The Dissertation Committee for Mark Bradley Powers Certifies that this is the approved version of the following dissertation:

Attributional Processes Concerning Medication Taking and Their Subsequent Effects on Fear Reduction during Exposure-based Treatment

Committee:

Michael J. Telch, Supervisor

Cindy Meston

James Pennebaker

Tim Schallert

Alexander Bystritsky

Attributional Processes Concerning Medication Taking and Their Subsequent Effects on Fear Reduction during Exposure-based Treatment

by

Mark Bradley Powers, B.A.; M.A.

Dissertation

Presented to the Faculty of the Graduate School of

The University of Texas at Austin

in Partial Fulfillment

of the Requirements

for the Degree of

Doctor of Philosophy

The University of Texas at Austin

May, 2006

Attributional Processes Concerning Medication Taking and Their Subsequent Effects on Fear Reduction during Exposure-based Treatment

Publication No._____

Mark Bradley Powers, Ph.D.

The University of Texas at Austin, 2006

Supervisor: Michael J. Telch

Abstract: The primary aim of the current study was to investigate the effects of attributions on fear reduction by having participants undergo exposure-based treatment in the context of an inactive medication that they were led to believe made the exposures easier (informed that the medication had a relaxing/sedating side-effect profile) or made the exposures more difficult (informed that the medication had an activating side-effect profile). Participants (N = 95) displaying marked claustrophobic fear were randomly assigned to 1 of 6 conditions: (a) Exposure Only (EO), (b) Exposure + Pill Placebo + Arousal

Instruction (EPA attribution for pill interference), (c) Exposure + Pill Placebo + Neutral Instruction (EPN), (d) Exposure + Pill Placebo + Relaxation Instruction (EPR attribution for pill facilitation), (e) credible psychological placebo treatment (PLT), or (f) wait-list (WL). Consistent with prediction, results showed that an attribution for pill facilitation (EPR: relaxing/sedating instruction) interfered with fear reduction and led to higher relapse. Contrary to prediction, an attribution for pill interference (EPA: arousal instruction) did not outperform the other exposure conditions. Clinically significant improvement rates at posttreatment were as follows: EO = 73%, EPA = 75%, EPN = 78%, EPR = 76%, PLT = 60%, WL = 10%. Clinically significant improvement rates at follow-up were as follows: EO = 87%, EPA = 85%, EPN = 89%, EPR = 53%, PLT = 40%, WL = 30%. Relapse rates at follow-up were as follows: EO=0%, EPA=0%, EPN=0%, and EPR=39%. The deleterious effects of the relaxation instructions were fully mediated by attributions about the helpful effects of the medication reducing the variance accounted for by treatment from 30% to 7%. Findings suggest the importance of assessing attributions during combined exposure-based and pharmacological treatments and attention to a slow medication taper and reapplication of exposure during the taper.

Table of Contents

CHAPTER 1: INTRODUCTION

The average anxiety disorder patient comes to treatment after having suffered with the disorder for 9 years and is likely taking medication. Fortunately, cognitive behavioral therapy (CBT) demonstrates some of the strongest effect sizes in the literature for treating anxiety. However, after successful CBT treatment many of these patients later relapse when they discontinue their medication. This is perplexing given the low relapse rates in similar patients who do not take medication during CBT. One possible explanation occurred to me while working with such patients. During the course of treatment patients would frequently ask, "I'm feeling much better lately, now what is going to happen if I stop taking my medication?" Clearly this patient is concerned that their treatment gains may partly be due to the medication and fear that discontinuing the medication may herald a return of symptoms. This question makes one wonder what role medication attributions play in explaining relapses. Is it possible that if a patient attributes their treatment gains to the medication that this will interfere with fear reduction? Preliminary studies suggest the answer could be yes. In this way patients may learn conditional safety – I'm ok as long as I take my medication. However, to date no study has experimentally manipulated attributions to test a causal relationship.

This study was designed to experimentally test the hypothesis that patients who undergo exposure-based treatment for anxiety while on medication may fair poorer at follow-up if they are medication free and attribute their gains to the medication rather than their own efforts and the exposure treatment. To test this hypothesis the study was designed to randomly assign participants to attribution for pill facilitation, attribution for pill interference, or a neutral attribution. We chose to conduct the study in the context of claustrophobia due to the fact that exposure treatment for this condition may be effective in only one session.

First, we describe the nature and treatment of specific phobias. Next we discuss the successes, but more importantly the failures of exposure-based treatment for anxiety disorders when they are paired with medication taking. Finally we describe a test of attributions as a possible explanation for treatment failure in combined treatment.

1.1 Defining Features of Specific Phobias

1.1.1 Nature and Epidemiology

According to the DSM-IV (American Psychiatric Association, 1994), the central feature of a specific phobia is a marked and persistent fear of a specific object or situation (e.g., animals, storms, seeing blood, enclosed spaces). Although recognizing that the fear is unrealistic and excessive, specific phobia sufferers avoid phobic situations or endure them with significant anxiety and distress. For those under 18-years old, the symptoms must last at least 6-months. Moreover, a DSM-IV diagnosis of specific phobia warrants that the fear and related avoidance cause significant interference with the normal routine, occupational functioning, or social activities and relationships.

The DSM-IV (American Psychiatric Association, 1994) makes a distinction between five subtypes: Animal Type (e.g., snakes, spiders, dogs), Natural Environmental Type (e.g., heights, storms, water), Blood-Injection-Injury Type, Situational Type (e.g., enclosed spaces, airplanes, elevators), and Other Type (e.g., choking, vomiting, or contracting an illness; in children, loud sounds or clowns).

Anxiety disorders have been estimated to be the most prevalent mental disorder. The National Comorbidity Survey Replication (NCS-R; Kessler, Berglund, Demler, Jin, & Walters, 2005; Kessler, Chiu, Demler, & Walters, 2005) with a sample of 9,282 English-speaking respondents aged 18 years or older and

based on DSM-IV criteria (American psychiatric Association, 1994) showed that 29% of the sample reported a lifetime history of at least one anxiety disorder (21% for any mood disorder) and 18% reported an anxiety disorder in the past 12 months (10% for any mood disorder).

Estimates of the lifetime and 1-year prevalence rates for specific phobias according to the DSM-IV from the National Comorbidity Survey Replication are about 13% and 9% respectively (American Psychiatric Association, 1994; Kessler, Berglund, Demler, Jin, & Walters, 2005; Kessler, Chiu, Demler, & Walters, 2005). A similar lifetime prevalence figure of 11% was reported in the earlier, ECA study (Eaton et al., 1991). However, anyone housing animals for treatment purposes finds that far more than 1 in 10 individuals express discomfort (in the laboratory alone). In fact, this is what other research suggests. The discrepancy lies in the definition and sample studied. Some studies have relied on a cutoff score on a continuum of severity in a community sample. For example, Agras, Sylvester, and Oliveau (1969) found that 25% of those interviewed in Burlington, Vermont reported an intense fear of snakes and 39% reported at least mild fear. In another community sample, Costello (1982) reported a higher prevalence of phobias (19%) in a sample of 449 women.

Specific phobias are approximately two to four times as common in women than in men. The lifetime and 1-month female-male prevalence ratios, respectively, are 2.3:1.0 (z=7.4, p<.05) and 3.8:1.0 (z=7.2, p<.05) (Magee, Eaton, Wittchen, McGonagle, & Kessler, 1996). The age of onset is most often in childhood (with the exception of claustrophobia having a mean onset age of 20-

years old) (Craske, 1999; *Öst*, 1987). More specifically, the age of onset for specific phobias typically ranges between an approximate mean of 4.4-years-old to 22.7-years-old (Marks and Gelder, 1966; Liddell and Lyons, 1978; Sheehan, Sheehan, and Minichiello, 1981; Thyer, Parrish, Curtis, Nesse, and Cameron, 1985). If phobias are defined as intense fears (endorsing "Terror" on fear items), an age pattern emerges (Kirkpatrick, 1984). Namely, as people approach old age, fears of heights and water increase, while fears of animals and insects decrease.

Phobia prevalence appears to be inversely related to education level and is higher among Hispanic populations, the unemployed (students, homemakers, etc), and those living with their parents or legal guardians (Magee, Eaton, Wittchen, McGonagle, & Kessler, 1996). In addition, phobias are equally distributed across income, region of the country, and urbanicity.

The course of specific phobias tends to be chronic with a low probability of spontaneous remission. The Munich Follow-up Study followed 1,366 subjects in the community from 1974 to 1981 and estimated that only 17 to 30% of the anxiety patients (n=77) experienced symptom remission (Wittchen, 1988). In addition, a study of patients seeking treatment for specific phobias suggested that participants had suffered from the fear for an average of 21-years, which is significantly higher than for the average pre-treatment duration of agoraphobic concerns (*Öst*, 1987).

Most people (83.4%) with a specific phobia report at least one other lifetime disorder (Magee, Eaton, Wittchen, McGonagle, & Kessler, 1996). The

most common comorbid conditions reported are: another anxiety disorder (68.7%), a mood disorder (46.8%), or substance-related disorders (39.4%).

1.1.2 Indirect and Direct Costs of Illness

The staggering costs of anxiety disorders have been well documented. Using the data from the NCS, Greenberg et al. (1999) estimated the total costs of anxiety disorders at 63.1 billion in 1998 dollars. This amount comprised medical treatment costs, psychiatric treatment costs, indirect workplace cost, and mortality costs. Further, anxiety disorders account for 31% of total annual mental health care costs, exceeding those due to mood disorders (22%) and schizophrenia (20%) (Rice & Miller, 1993). This figure is elevated due to the high prevalence, chronic nature, and functional impairment of anxiety.

Anxiety disorders are also associated with an increased use of welfare, impaired marital and social functioning (Markowitz, Weissman, Ouellette, Lish, & Klerman, 1989), and impaired work productivity and employment status (Edlund & Swann, 1987). Further, the quality of life in outpatients with panic disorder may be impaired as much as in patients with hypertension, diabetes type 2, chronic obstructive pulmonary disease and osteoarthritis (Candilis, McLean, Otto, Manfro, Worthington, Paneva, Marzol, & Pollack, 1999). In addition, the suicide rate for inpatients with anxiety disorders is as high as for inpatients with mood disorders (Allgulander & Lavori, 1991). In one study of people suffering from specific phobias, 34.2% reported significant interference, 30.2% sought professional help, and 8% reported lifetime use of medications for their phobias (Magee, Eaton, Wittchen, McGonagle, & Kessler, 1996). Most patients, however,

do not seek help. Only 16 to 40% of anxiety patients seek appropriate treatment due to avoidance and misdiagnosis, resulting in reduced work productivity, unnecessary medical procedures, and poor medication management (Angst & Dobler-Mikola, 1985; Thompson, Burns, Bartko, Boyd, Taube, & Bourbon, 1988; Pollard, Henderson, Frank & Margolis, 1989). So the actual cost (including direct and indirect) of anxiety disorders may be much higher than estimated.

1.2 Etiology of Specific Phobias

Researchers currently agree that phobias are caused by a combination of both biological and environmental influences. These influences may include conditioning (e.g., experiencing a car accident), modeling and vicarious experiences (e.g., seeing another person experience a car accident or repeatedly watching someone else behave fearfully while driving), and information transmission (e.g., reading or hearing about the dangers of driving; Rachman, 1976, 1977). Many studies have supported these methods of acquisition (e.g., Di Nardo et al., 1988; Ehlers, Hofmann, Herda, & Roth, 1994; McNally & Steketee, 1985; Menzies & Clarke, 1993a; Merchelbach, Arntz, & de Jong, 1991; Merchelbach, Arntz, Arrindell, & de Jong, 1992; Merchelbach & Murris, 1997; Muris, Merchelbach, & Collaris, 1997; Muris, Steerneman, Merchelbach, & Meesters, 1996; Öst, 1985, 1991; Öst & Hugdal, 1985; Rimm, Janda, Lancaster, Nahl, & Dittmar, 1977; Townend, Dimigen, & Fung, 2000). Specifically, evidence has accumulated for animal fears (Fredrikson, Annas, & Wik, 1997; King, Clowes-Hollins, & Ollendick, 1997; Merckelbach, Arntz, Arrindell, & de Jong, 1992; Merckelbach, Arntz, & de Jong, 1991; Öst & Hugdahl, 1981),

claustrophobia (Öst & Hugdahl, 1981), dental and blood, injury, and injection phobia (de Jongh, Muris, ter Hurst, & Duyx, 1995; Kleinknecht, 1994; Moore, Brodsgaard, & Brin, 1991; Öst, 1991; Öst & Hugdahl, 1985), and driving phobia (Munjack, 1984). However, studies of environmental influences may lack reliability as they most often rely on retrospective self-reports. For example, Taylor, Deane, and Podd (1999) found that participants often reported a different method of fear acquisition when asked one-year later. In addition, between 5% and 25% of cases people are unable to recall how they acquired their fears (Rachman, 1990). For these reasons, it is difficult to estimate the contribution of environmental factors.

1.2.1 Biological Vulnerability

Research on biological contributions to the etiology of mental disorders rely on family studies, twin studies, and identification of single and multiple gene effects. These methods generate estimates of heritability and relative risk. Uhl, Gold, and Risch (1997) state, "Heritability reflects the proportion of the total interindividual variation due to a gene variant, reflecting both the gene variant's frequency in the population and the size of the effects that the gene variant causes. Sibling relative risk assesses the increased disease risk to siblings that share one-half of the genes with affected probands." Heritability estimates are most often reported as either correlations (for continuous traits such as height or IQ) or concordances (for categorical traits such as mental disorders) (Willerman and Cohen, 1990).

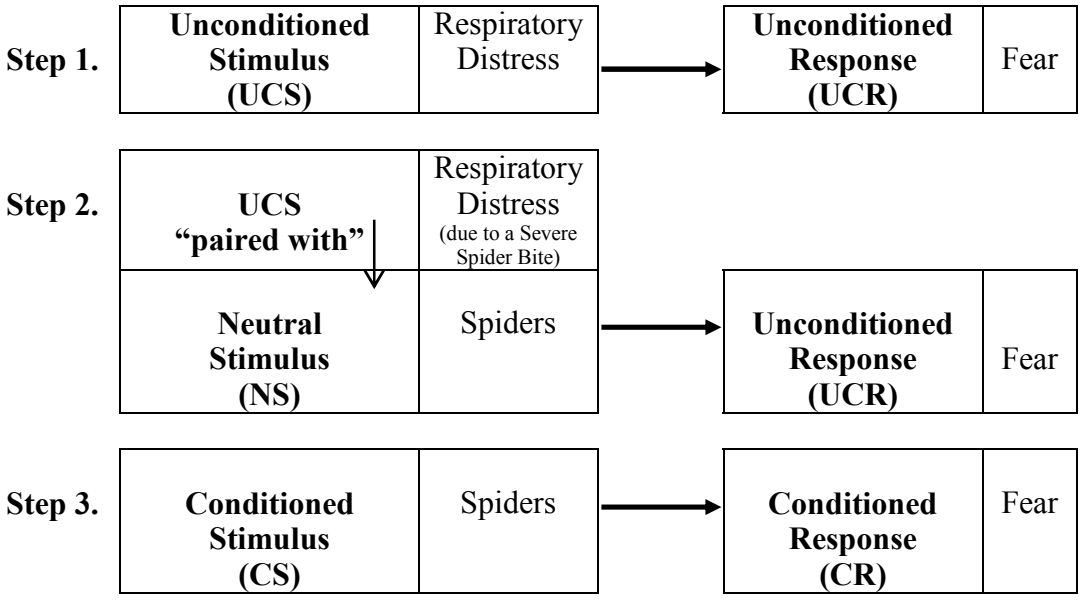
FAMILY STUDIES. Data suggest that specific phobias tend to run in families (Fredrikson, Annas, and Wik, 1997; Fyer, Mannuzza, Gallops, Martin, Aaronson, Gorman, Leibowitz, & Klein, 1990). Further, there is a significant correlation between children's fears and the extent to which their mothers exhibit their fears (Muris, Steerneman, Merckelback, and Meesters, 1996). Fyer et al. (1990) investigated 49 first-degree relatives of probands and 119 relatives of controls and found a specific phobia relative risk of 3.3 (31% in relatives of probands vs. 13% in relatives of controls). Likewise, Fredrickson et al. (1997) also found an increased risk in relatives of probands compared to controls. However, due to the correlational nature of Family studies, these data offer little unique information on what is causing the higher than expected incidence of phobias within families.

TWIN STUDIES. Heritability estimates in twin studies for anxiety range between 19 and 50% (Clifford, Hopper, Fulker, and Murray, 1984; Jardine, Martin, and Henderson, 1984; Kendler, Walters, Neale, Kessler, Heath, and Eaves, 1995; MacKinnon, Henderson, and Andrews, 1990). For example, Kendler, Neale, Kessler, Heath, and Eaves (1992) found concordance rates for animal phobias among monozygotic and dizygotic twins of 26% and 11% respectively. Similarly, they later found differential concordance rates for situational and blood-injection-injury phobias (Kendler, Karkowski, and Prescott, 1999). More specifically, they found heritability estimates of: animal 47%, blood/injury 59%, and situational 46%.

GENE IDENTIFICATION. Studies of genetic contributions to mental disorders suggest two conclusions: (a) there may be a general gene for neurotic mental illness, and (b) unique environment may determine which mental disorder develops and when. Kendler, Heath, Martin, & Eaves (1987) found that genetics accounted for 27% of the total variance in anxious and depressive symptoms. These studies tell us there is not a single vulnerability for developing an anxiety disorder. Rather, there may be a general genetic vulnerability to develop either anxiety or depression (Kendler, Heath, Martin, & Eaves, 1987; Kendler, Neale, Kessler, Heath, & Eaves, 1992; Kendler, 1996). Further, some research has demonstrated a shared genetic risk of developing multiple neurotic disorders with unique environment determining which disorder evolves (Kendler, Walters, Neale, Kessler, Heath, & Eaves, 1995). More specifically, animal studies have determined that areas on chromosomes 1, 12, and 15 create a general tendency to be anxious (Flint, Corley, DeFries, Fulker, Gray, Miller, & Collins, 1995). Future studies will help determine if this finding generalizes to humans.

1.2.2 Conditioning Experiences (direct, traumatic)

Direct or traumatic accounts of phobia etiology posit that people experience a fear reaction (UCR) in the presence of a particular situation or object (NS, e.g. a spider) paired with a noxious stimulus (UCS, a severe bite with respiratory distress). Eventually, the person experiences fear (CR) from the conditioned stimulus (CS) alone (see figure).



But according to this theory we would expect that the fear would simply extinguish after enough experiences with spiders in the absence of another serious bite. This lead Mowrer (1960) to develop the two-factor theory whereby the fear is acquired through classical conditioning and then maintained by operant conditioning (escape/avoidance of spiders). Rates of people reporting direct traumatic experiences with the phobic object or situation are as follows: animal fears = 26.7 to 67% (Fredrikson, Annas, & Wik, 1997; King, Clowes-Hollins, &

Ollendick, 1997; Merckelbach, Arntz, Arrindell, & de Jong, 1992; Merckelbach, Arntz, & de Jong, 1991), claustrophobia = 69% (Öst & Hugdahl, 1981), dental and blood, injury, and injection phobias = 49 to 69% (de Jongh, Muris, ter Horst, & Duyx, 1995; Kleinknecht, 1994; Moore, Brodsgaard, & Brin, 1991; Öst, 1991; Öst & Hugdahl, 1985), and fears of driving = 70% (Munjack, 1984). Children report direct conditioning experiences more than any other acquisition pathway (40%; Muris, Merckelbach, & Collaris, 1997).

1.2.3 Modeling or Vicarious Experiences

Conditioning theories of phobias make sense given the face validity and success of behavioral interventions in treating them. However, data are mixed supporting this theory as the *only* explanation for phobia development. Rachman (1990) stated, "By 1977, it had become clear that conditioning theory was incomplete and that there was a need to identify other forms of fear acquisition". Rates of people reporting modeling or vicarious experiences by type of phobia are as follows: animal fears = 28 to 71% (Fredrikson, Annas, & Wik, 1997; King, Clowes-Hollins, & Ollendick, 1997; Merckelbach, Arntz, Arrindell, & de Jong, 1992; Merckelbach, Arntz, & de Jong, 1991), claustrophobia = 9% (Öst & Hugdahl, 1981), dental and blood, injury, and injection phobias = 12% (de Jongh, Muris, ter Horst, & Duyx, 1995; Kleinknecht, 1994; Moore, Brodsgaard, & Brin,

1991; Öst, 1991; Öst & Hugdahl, 1985). Children report modeling experiences in only 1% of cases (Muris, Merckelbach, & Collaris, 1997).

1.2.4 Information Transmission

Interestingly, people can even acquire irrational fears in the absence of direct or vicarious experience. Misinformation regarding threats is also a popular reported mechanism of phobia onset. Rates of people reporting information transmission by type of phobia are as follows: animal fears = 6.7 to 15% (Fredrikson, Annas, & Wik, 1997; King, Clowes-Hollins, & Ollendick, 1997; Merckelbach, Arntz, Arrindell, & de Jong, 1992; Merckelbach, Arntz, & de Jong, 1991), claustrophobia = 11% (Öst & Hugdahl, 1981), dental and blood, injury, and injection phobias = 6% (de Jongh, Muris, ter Horst, & Duyx, 1995; Kleinknecht, 1994; Moore, Brodsgaard, & Brin, 1991; Öst, 1991; Öst & Hugdahl, 1985). Children reported information transmission as the cause of their fear onset in 27% of cases (Muris, Merckelbach, & Collaris, 1997).

In summary, specific phobias appear to develop as a combination of biological vulnerability and experience. See Figure 1 and Figure 2 for diagrams of the proposed etiology of specific phobia.

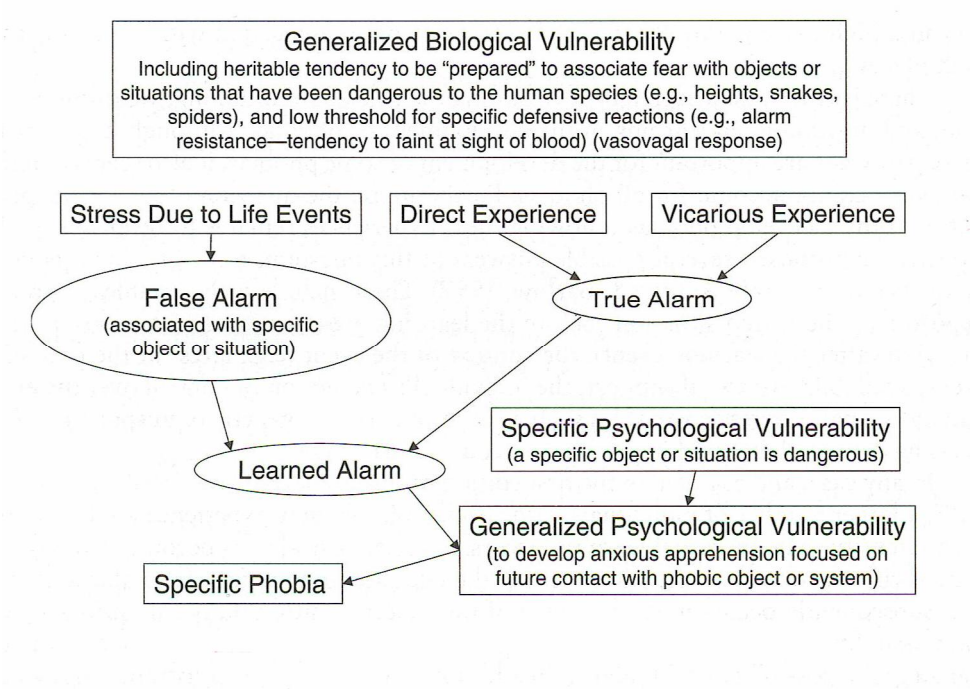


Figure 1. A model of the various pathways to a specific phobia. *Source*: Barlow (2002)

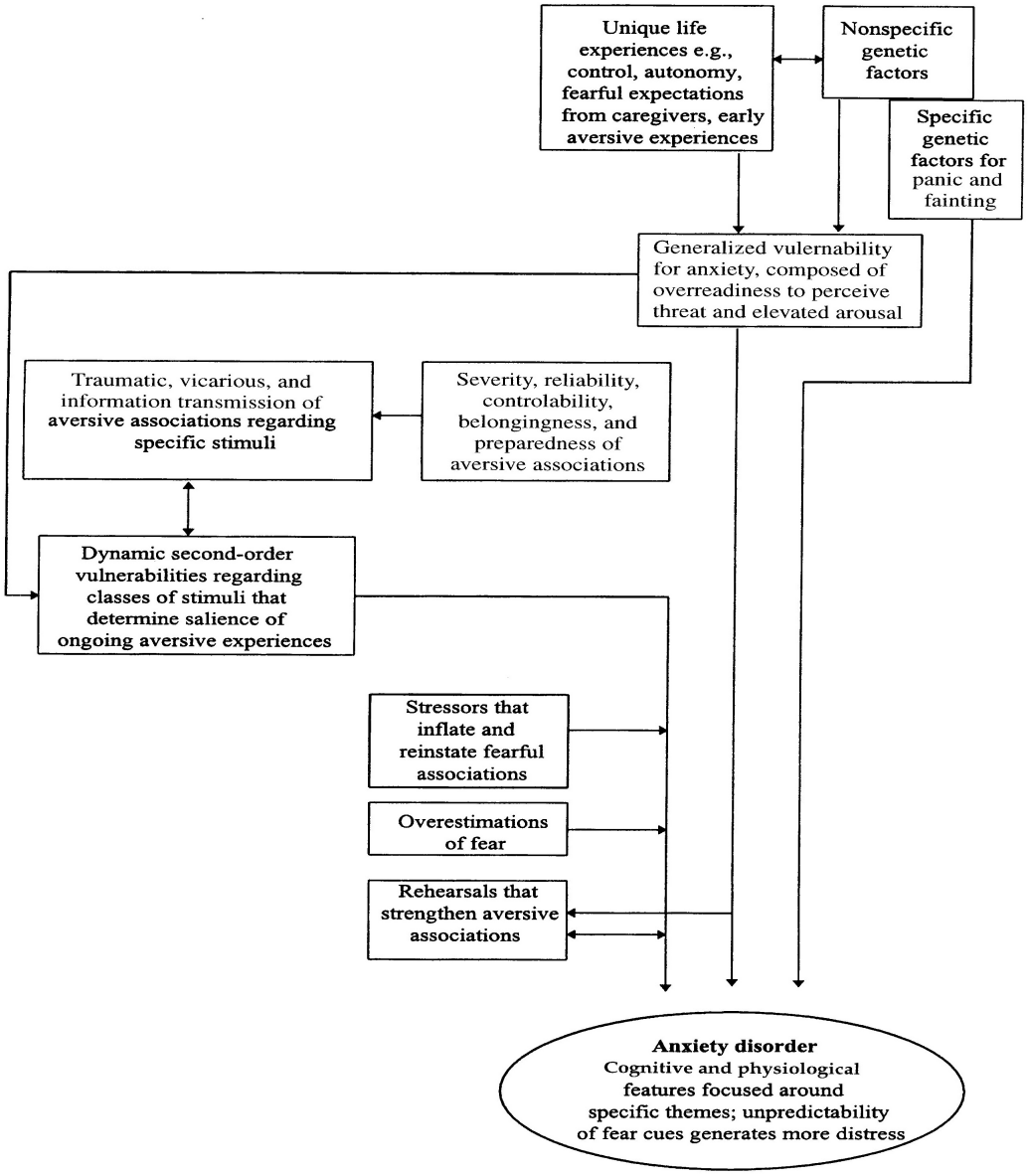


Figure 2. Summary of etiological factors contributing to the anxiety disorders. (*Source:* Craske, 1999)

1.3 Treatment Approaches for Specific Phobias

1.3.2 Psychosocial

1.3.2.1 Exposure-Based Treatment

Exposure-based treatments are currently considered the treatments of choice for specific phobias. They were first developed during the Second World War to treat combat PTSD (Wolpe, 1958, 1973). Joseph Wolpe, a South African doctor, complained of the poor efficacy of psychodynamic therapy in treating what was then called "shell shock". He wrote to his mentor at Johannesburg and asked if he could return to develop a better treatment for anxiety disorders. He first developed an animal model of neurotic anxiety by shocking cats in their cages based on previous work by Pavlov. The cats were so frightened that they would starve to death before eating in that cage again. Wolpe then assumed that fear and feeding were incompatible. Therefore, he assumed that if he could either raise the hunger or lower the anxiety of the cats, that the feeding response would take over and inhibit the fear. Raising the hunger was not an option, as mentioned above, the cats were so frightened that they would starve before eating in the original cage. He tried lowering the anxiety by changing the surroundings to be less like the learning environment. This was done by changing cages, rooms, and furniture. Success! The cats would first look around hesitantly in the new surroundings, and then slowly begin to sniff at and eventually eat the meat pellets enthusiastically. Next, he would add the furniture back and the same process occurred, first hesitation followed by voracious feeding. Finally he had the cat eating back in the original room and in the original cage. He came to call this

systematic desensitization and assumed the mechanism of change was due to what he coined “reciprocal inhibition”.

Wolpe (1990) wrote, “We saw that strong evocations of anxiety were associated with inhibition of eating in food-deprived neurotic cats. By contrast, eating took place when anxiety was relatively weak, and repeated eating resulted in manifest diminutions of the anxiety. A reciprocally inhibitory relationship between the two responses was thus apparent…”. Systematic desensitization involves teaching a patient to relax while exposing them to fearful images that gradually increased in intensity. Today, exposure therapy may be defined as “A form of behaviour therapy in which individuals are required to confront the object or situation that they fear. Typically, exposure is conducted in a structured and predictable manner and is repeated frequently.” (Antony and Swinson, 1996). In addition, modern exposure therapy is most often conducted in-vivo whenever possible. This is due to three primary reasons. First, some studies have found in-vivo exposure to be even more effective than imaginal exposure (Emmelkamp & Wessels, 1975; Mannion & Levine, 1984). Second, in-vivo exposure requires fewer sessions. Finally, data suggest there may be no additional benefit of adding relaxation training to exposure-based treatments (Öst, Lindahl, Sterner, & Jerremalm, 1984).

To date, in-vivo exposure has been found to be effective for the treatment of spiders (Hellstrom and Öst, 1995; Muris, Mayer, and Merckelbach, 1998; Öst, 1996b; Öst, Ferebee, and Furmark, 1997; Öst, Salkovskis, and Hellstrom, 1991), snakes(Gauthier and Marshall, 1977; Hepner and Cauthen, 1975; Hepner and

Cauthen, 1975), rats (Foa, Blau, Prout, and Latimer, 1977), thunder and lightening (Öst, 1978), water (Menzies and Clarke, 1993b), heights (Baker, Cohen, and Saunders, 1973; Bourque and Ladouceur, 1980), flying (Beckham, Vrana, May, Gustafson, and Smith, 1990; Howard, Murphy, and Clarke, 1983; Öst, Brandberg, and Alm, 1997), enclosed spaces (Öst, Johansson, and Jerremalm, 1982; Craske, Mohlman, Yi, Glover, and Valeri, 1995; Powers, Smits, and Telch, 2004), choking (Greenberg, Stern, and Weilburg, 1988), dental fears (Gitin, Herbert, and Schmidt, 1996; Moore and Brodsgaard, 1994), blood (Öst, Fellenius, and Sterner, 1991), and balloons (Houlihan, Schwartz, Miltenberger, and Heuton, 1993).

1.3.2.2 Cognitive Therapy

Although exposure-based treatments are considered to be the gold standard for treating specific phobias, cognitive approaches are also effective (Craske and Rowe, 1997). Cognitive therapy can be defined as "A form of psychological treatment that attempts to change the thoughts which maintain a psychological disorder. Examples of cognitive therapy techniques include cognitive restructuring, and coping self-statements." (Antony and Swinson, 1996). Barlow and Durand (1995) further suggest that cognitive therapy is a "Treatment approach that involves identifying and altering negative thinking styles related to psychological disorders such as depression and anxiety and replacing them with more positive beliefs and attitudes and, ultimately, more adaptive behavior and coping styles". To date, cognitive therapy has proven effective for fears of enclosed spaces, spiders, snakes, and dental phobias (de Johgn, Muris, Horst, van Zuuren, Schoenmakers, and Makkes, 1995; Jerremalm, Janson, and Öst, 1986;

Getka and Glass, 1992; Craske, Mohlman, Yi, Glover, and Valeri, 1995; Booth and Rachman, 1992). Although these studies suggested that cognitive interventions are effective, there was no evidence that they outperformed exposure-based treatments. In addition, although the best outcomes may arise from *in vivo* exposure, recent mediation studies suggest that the mechanism of action in anxiety disorder treatment may be cognitive change (Smits, Powers, Cho, and Telch, 2004; Hofmann, in press). This has led some to suggest that cognitive strategies may best be applied as an addition to exposure-based treatment to enhance outcome (Panzarella and Garlipp, 1999; Antony and Swinson, 2000).

1.3.2.3 Alternative Approaches

The two main alternative approaches to treating specific phobias include Eye Movement Desensitization and Reprocessing (EMDR) and applied tension for blood-injection-injury phobias.

E.M.D.R. EMDR may be defined as "A new form of exposure therapy that has been a source of controversy in the behavior therapy literature. While visualizing a feared image, individuals track the rapid movements of a therapist's finger back and forth across the image. Proponents of this approach believe that this is a unique therapeutic modality. Critics argue that the effects of this technique are attributable entirely to the exposure component." (Antony and Swinson, 1996). EMDR was originally intended for the treatment of trauma (Shapiro & Forrest, 1997). More recently, EMDR has been used to treat multiple anxiety disorders including specific phobias. However, studies with phobic

participants suggest that: (a) EMDR is only effective in reducing subjective fear ratings and not behavioral performance (Muris, Merckelbach, Holdrinet, & Sijsenaar, 1998; Muris, Merckelbach, van Haaften, & Mayer, 1997), (b) the active component in EMDR is imaginal exposure (Sanderson & Carpenter, 1992), and (c) EMDR is not as effective as *in vivo* exposure (Muris, Merckelbach, Holdrinet, & Sijsenaar, 1998; Muris, Merckelbach, van Haaften, & Mayer, 1997).

APPLIED TENSION. Applied tension is a method of treating individuals with blood or injection phobias who tend to faint in the feared situation. Individuals are taught to tense the muscles of their body in order to raise their blood pressure and thereby prevent fainting in the presence of blood or injections. These skills are integrated with exposure to feared cues as they are practiced while confronting increasingly difficult situations." (Antony and Swinson, 1996).

1.3.3 Pharmacological Treatment

There is good evidence that anxiety disorder patient respond well to monoamine oxidase inhibitors (MAO-I), selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants, and benzodiazepines (Lydiard, Brawman-Mintzer, & Ballenger, 1996; Pollack & Smoller, 1996). However, when such patients discontinue their medication relapse is common (Noyes, Garvey, Cook, & Samuelson, 1989; Noyes, Garvey, Cook, & Suelzer, 1991; Pollack & Smoller, 1996). In addition, studies of panic disorder suggest that the longer a patient stays on their medication the better the outcome (Mavissikalian & Perel, 1993). To date, it is generally accepted that medications are not helpful for patients with specific phobias. However, due to the disabling nature of specific phobias

(Magee, Eaton, Wittchen, McGonagle, & Kessler, 1996) and the fact that phobics react to CO_2 similarly to those with panic disorder (Verburg, Griez, & Meijer, 1994) have led some to believe that pharmacotherapy may be helpful. Studies including benzodiazepines during standard treatment have suggested either no additional benefit (Whitehead, Robinson, Blackwell, and Stutz, 1978; Zoellner, Craske, Hussain, Lewis, and Echeveri, 1996) or only short term efficacy (Wilhelm and Roth, 1997; Thom, Sartory, and Johren, 2000). Research on selective serotonin reuptake inhibitors (SSRIs) has also been conducted. A case study of two participants being treatment for depression suggested that fluoxetine may have been effective in reducing fears of flying (Abene and Hamilton, 1998). In addition, Benjamin, Ben-Zion, Karbofsky, and Dannon (2000) conducted a preliminary double-blind placebo-controlled study of paroxetine for specific phobias (n=11). Response rates for SSRI and placebo conditions were 60% and 17% respectively. Again, follow-up assessments were not conducted to determine the durability of the findings.

1.3.4 Combined CBT and Pharmacotherapy

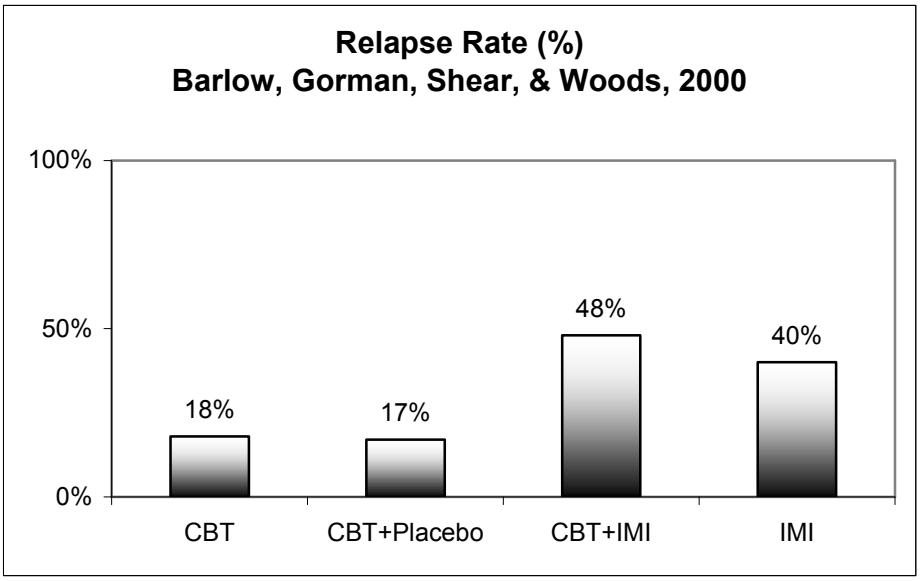
Some researchers have considered the possibility that combining two effective treatments may enhance outcome (see Telch et al., 1985 and Telch & Lucas, 1994 for reviews). This lead to the investigation of combined cognitive behavioral and pharmacological treatment of anxiety disorders. Combination treatments have not been previously investigated in specific phobias. However, some studies show advantages of combined treatment over monotherapy after acute treatment for panic disorder (Barlow, Gorman, Shear, and Woods, 2000;

Marks et al., 1993), social phobia (Blomhoff, et al., 2001), OCD (Hohagen et al., 1998; Cottraux et al., 1990), and GAD (Power, Simpson, Swanson, & Wallace, 1990). Other studies do not show such an advantage (Franklin, Abramowitz, Bux, Zoellner, & Feeny, 2002; van Balkom et al., 1998; Gould et al., 1995). In addition, some studies suggest that the advantage of combined treatment may be accounted for by pill taking alone (Barlow et al., 2000; Power et al., 1990). However, long-term follow-up assessment suggests either no advantage or worse outcome for patients receiving combined treatment than those receiving CBT alone in panic disorder (Barlow, et al., 2000; Marks et al., 1993) and social phobia (Huag et al., 2003). Some authors have suggested that the deleterious effects of combined treatments may be due to attributions to the positive effects of medications that are lost once medication is discontinued (Basoglu, Marks, Kilic, & Brewin, 1994; Telch & Lucas, 1994). Although simultaneous combination treatment may prove less effective in the long run, there is some evidence that if patients fail to respond to one treatment that switching to the other modality may be helpful. For example, panic disorder and PTSD patients who fail to respond to an adequate trial of pharmacotherapy may later improve with CBT (Otto, Pollack, Paneva, & Zucker, 1999; Pollack, Otto, Kaspi, Hammerness, & Rosenbaum, 1994; Otto et al., 2003). Likewise, panic patients that do not respond to CBT may later improve with pharmacotherapy (Kampman, Keijsers, Hoogduin, & Hendriks, 2002; Fava et al, 1997).

CHAPTER 2: THE PRESENT STUDY

2.1 Introduction

Although combined treatment is frequently used in the treatment of anxiety disorders, evidence suggests that for at least some anxiety disorders, the combination of medication plus CBT may result in greater relapse (return of fear) than CBT alone (see Figure: Barlow, Gorman, Shear, & Woods, 2000; Marks et al., 1993).



One possibility to account for this finding is that medication taking for anxiety disorders can be conceptualized within the framework of safety behavior theory. Anxiety-maintaining safety behaviors consist of actions that people perform when confronting fear-provoking situations in an effort to avert or attenuate a perceived

threat (Kamphuis & Telch, 1999). These behaviors may be covert (e.g., distraction) or overt (e.g., carrying or ingesting rescue medication). Paradoxically, the use of such safety-behaviors during exposure to fear-provoking cues has been shown to undermine the therapeutic efficacy of exposure (Sloan & Telch, 2001). Misattributional processes have been proposed as one possible factor accounting for the disruptive effects of safety behaviors on fear reduction during exposure (Salkovskis, 1991; Basoglu, Marks, Kilic, & Brewin, 1994; Telch, Tearnan & Taylor, 1983; Telch & Lucas, 1994).

The overall goal of this study was to shed light on how attributional processes influence the effects of medication taking on subsequent return of fear (ROF) following exposure-based treatment. Participants meeting DSM-IV criteria for specific phobia with primary claustrophobia complaints were randomly assigned to one of six treatment conditions: (a) Exposure Only – no pill (EO), (b) Exposure + Pill Placebo with Arousal expectation (EPA), (c) Exposure + Pill Placebo with relaxation expectation (EPR), (d) Exposure + Pill Placebo with neutral expectation (EPN), (e) credible non-pill placebo treatment (PLT), or (f) wait-list (WL). In each of the exposure + pill conditions, participants were told that the pill was adomoxin (a fictional herbal supplement) and that one aim of the experiment is to test whether the pill enhances later recall memory for treatment. Upon completing treatment, participants in the EPR condition were told that adomoxin has a sedating side-effect profile that should have made the exposures

much easier; whereas participants in the EPA condition were told that adomoxin has an activating side-effect profile that should have made the exposures much more difficult. The EPN participants were told that they received a placebo (Vitamin C) that should have had no effect on their treatment. The effect of this pill attribution manipulation on return of fear at a one-week follow-up was assessed.

2.2 Specific Aims

Aim 1. Test the effects of an attributional manipulation in which participants were led to believe that their improvement during treatment occurred in the context of having taken a pill that made their exposure therapy less anxiety-provoking and hence less difficult (i.e., I was able to conquer the chamber because I was sedated by the pill). **Hypothesis 1.** The Exposure-Pill placebo + Relaxation instruction group (EPR) would show less overall improvement and higher return of fear at follow-up compared to the other exposure conditions.

Aim 2. Test the effects of an attributional manipulation in which participants were led to believe that their improvement during treatment occurred in the context of having taken a pill that made their exposure therapy more anxiety-provoking and hence more difficult (i.e., I was able to conquer the chamber despite being "wired by the pill).

Hypothesis 2. The Exposure-Pill placebo + Arousal instruction group (EPA) would show greater overall improvement and lower return of fear at follow-up compared to the other exposure conditions.

Aim 3. To further examine the specificity of exposure-based treatments through the inclusion of both placebo and waitlist conditions.

Hypothesis 3. All of the active-treatment groups would outperform the placebo treatment group. The placebo group would outperform the wait-list condition.

Aim 4. Determine if differences in response were mediated by attributions to the medication as a manipulation check.

Hypothesis 4. The reduced fear reduction in the EPR condition would be mediated by medication attributions.

Aim 5. To examine the potential moderating effects of age, gender, diagnostic status, and ethnicity in predicting participants' response to treatment.

Hypothesis 5. Based on previous studies from this laboratory, findings would not be moderated by age, gender, diagnostic status, or ethnicity.

2.3 Background and Significance

The continuum from *worry* through *anxiety* to *panic***,** functions as an essential human motivator. These are three responses to perceived threat that vary according to the proximal nature of the threat. Anxiety motivates people to

meet deadlines and panic may prevent immediate catastrophes. As Howard Liddell (1949) stated, "Anxiety is the shadow of intelligence". Unfortunately, many Americans perceive threat that far exceeds any real danger to the point of significant avoidance and life impairment that can then be called an anxiety *disorder***.**

The Problem. Anxiety disorders cost the United States economy $63 billion each year (Greenberg, Sisitsky, Kessler, Finkelstein, Berndt, Davidson, Ballenger, & Fyer, 1999). This accounts for 31% of total annual mental health care costs, exceeding those due to mood disorders (22%) and schizophrenia (20%) (Rice & Miller, 1993). This figure is elevated due to the high prevalence, chronic nature, and functional impairment of anxiety disorders. Anxiety disorders have been estimated to be the most prevalent mental disorder. The National Co-morbidity Survey (NCS; Kessler et al., 1994) with a sample of 8,098 15 to 54-year-olds and based on DSM-III-R criteria (American psychiatric Association, 1987) showed that 25% of the sample reported a lifetime history of at least one anxiety disorder (20% for any mood disorder) and 17.2% reported an anxiety disorder in the past 12 months (11% for any mood disorder). The probability of spontaneous remission of symptoms for patients with anxiety is low. The Munich Follow-up Study followed 1,366 subjects in the community from 1974 to 1981 and estimated that only 17 to 30% of the anxiety patients (n=77) experienced symptom remission (Wittchen, 1988). Anxiety disorders predict increased use of

welfare, impaired marital and social functioning (Markowitz, Weissman, Ouellette, Lish, & Klerman, 1989), and impaired work productivity and employment status (Edlund & Swann, 1987). In addition, the suicide rate for inpatients with anxiety disorders is as high as for inpatients with mood disorders (Allgulander & Lavori, 1991). Most patients, however, do not seek help. Only 16 to 40% of anxiety patients seek appropriate treatment due to avoidance and misdiagnosis, resulting in reduced work productivity, unnecessary medical procedures, and poor medication management (Angst & Dobler-Mikola, 1985; Thompson, Burns, Bartko, Boyd, Taube, & Bourbon, 1988; Pollard, Henderson, Frank & Margolis, 1989). So the actual cost (including direct and indirect) of anxiety disorders may be much higher than estimated.

The Good News. Many studies have demonstrated the efficacy of cognitive behavior therapy (CBT) in treating anxiety disorders (Craske, 1999; Barlow, 1988; Marks, 1978). For instance, in 10 controlled studies of cognitive-behavioral therapy for specific phobias, an average of 76% of participants improved after only 4.8 hours of therapy (Arntz & Lavy, 1993; Hellstrom, Fellenius, & Öst, 1996; Hellstrom & Öst, 1995; Öst, 1996; Öst, Fellenius, & Sterner, 1991; Öst, Ferebee, & Furmark, 1997; Öst, Hellstrom, & Kaver, 1992; Öst et al., 1982; Öst, Salkovskis, & Hellstrom, 1991; Öst, Sterner, & Fellenius, 1989). This figure rose to 78% after 11 months and the attrition rate was only 2%.

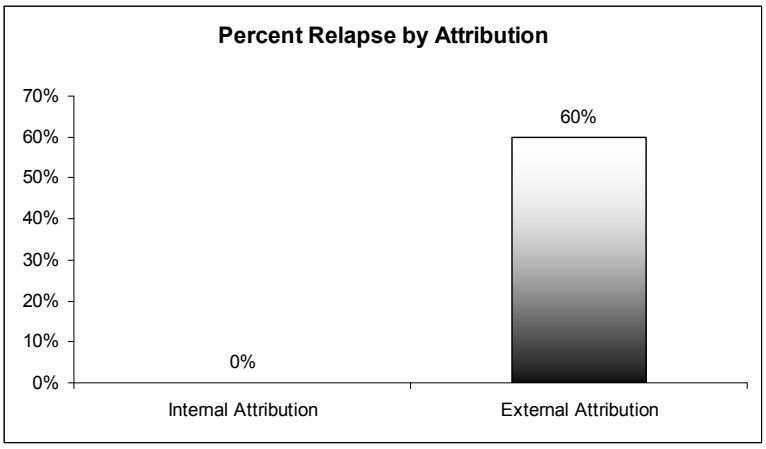
The Bad News. Unfortunately, not all patients respond to CBT (5-50%) and up to 20% of anxiety patients will relapse within 6 months of CBT cessation (Barlow, Gorman, Shear, & Woods, 2000). Furthermore, as mentioned above, only 16 to 40% of anxiety patients seek appropriate treatment due to avoidance and misdiagnosis. This may be due to practitioners and patients alike not being adequately educated regarding effective treatments. In one study, 76% of claustrophobics who sought treatment reported that they would have sought treatment earlier if they had known effective non-pharmacological methods were available (Rachman, 1990).

Reasons for Non-Responders and Relapse (Safety Behaviors). Given these fluctuations in treatment response, it is important to understand the theories of fear reduction and the mechanisms involved in the maintenance of fear. A comprehensive conceptualization of the factors involved in the maintenance of fear was suggested by Salkovskis and colleagues (1991). Salkovskis' suggested that safety behaviors, which can be any of a variety of behaviors (e.g. avoidance, escape, taking or carrying medication, cognitive distraction, sitting down to prevent fainting, or blending food to prevent choking) that are perceived as actively preventing a feared outcome, will prevent threat disconfirmation. Our pilot research suggests that safety behaviors do, in fact, exert a detrimental effect on fear reduction (see below). At least four theories have been suggested that may explain why safety behaviors interfere with fear reduction: 1) diminished

cognitive resources (Sloan & Telch, 2001), 2) the threat transmission model (Sloan & Telch, 2001, and 3) context effects (Powers, Smits, & Otto, 2005), and 4) misattribution of safety to the safety behavior **(**Salkovskis, 1991). The current study is intended to rigorously test the misattribution theory of how safety-behaviors exert their detrimental effects on fear reduction.

Attribution Theory and Combined Treatments Attribution theory describes how people explain events and the behavioral and emotional consequences of those explanations. In his book *The Psychology of Interpersonal Relationships,* Fritz Heider referred to attribution theory as "naïve" psychology (Heider, 1958). In two separate reviews of combined treatments for panic disorder/agoraphobia, Telch, Tearnan, and Taylor (1983) and Telch (1988) discussed the possibility that combining medications and Exposure may lead to an undermining of personal mastery due to external attribution effects. More recently, attribution theory has been applied to the study of combined medication and CBT relapse (Basoglu, Marks, Kilic, & Brewin, 1994; D. Barlow, personal communication, March 6, 2003; Biondi, & Picardi, 2003; Marks, et al., 1993). Basoglu, Marks, Kilic, and Brewin (1994) investigated the role of attribution in predicting relapse in patients treated with medication (alprazolam or placebo) plus CBT (exposure or relaxation). They found that attributions of improvement to the medication (alprazolam or placebo) predicted relapse. However, they did not include an exposure only condition, nor did they control for specific instructions

describing the effects of the medication. Barlow, Gorman, Shear, & Woods (2000) found that participants successfully treated with CBT + medication relapsed upon medication discontinuation. S. Raffa and D. Barlow (personal communication, March 6, 2003) suggested that misattribution of treatment gains to the medication may help explain the high relapse rate among participants in combination treatments. Biondi and Picardi (2003) found that 60% of participants who made external/medication attributions in a combination treatment relapsed, whereas, no participants relapsed who made internal attributions (see figure).



Biondi and Picardi (2003)

Is it possible to manipulate attributions? Placebo + Instructional Set Manipulation Research. In a classic study, Storms and Nisbett (1970) administered pill-placebos to 42 insomniacs shortly before going to bed. Some participants were told that the pills would cause arousal, while others were told to

expect sedation. Consistent with their reverse placebo effect prediction, participants in the arousal condition experienced reduced sleep onset latency on the evenings that they ingested the "arousal" pills. Storms and Nisbett (1970) hypothesized that this was because the participants had attributed their arousal to the pills rather than to their emotions. However, these findings have not been replicated by others (Kellogg & Baron, 1975; Bootzin, Herman, & Nicassio, 1976; Heffler, and Lisman, 1978). In fact, these replication failures suggested a straightforward placebo effect. Likewise, previous findings with exposure-based anxiety treatments demonstrate that the administration of a placebo prior to exposure treatment combined with bogus "stimulant" or "sedative" side effect profile descriptions, results in treatment outcome consistent with their instructional set (i.e. participants told that they are being given a stimulant experience less fear reduction whereas sedative instructions result in greater fear reduction) (Singerman, Borkovec, & Baron, R.S., 1976; Holroyd, 1978). Furthermore, removal of the placebo results in an effect opposite to the stimulant or sedative manipulations (i.e. return of fear in the sedative instruction group). This line of research was originally intended to produce a "reverse placebo" effect with anxiety patients. However, consistent with the replication failures mentioned above, the research supports a straightforward placebo effect. Therefore, this model may be applied to the study of treatment-relevant attributions.

The previous research leads to four primary questions:

1) Do safety behaviors (such as taking medication) interfere with fear reduction?
2) Does the reduction of the utilization of these behaviors increase the efficacy of CBT treatment?
3) Do these behaviors interfere only when they are used? or do they even exert a detrimental effect when they are perceived as available (i.e. carrying medication but not taking it)?
4) How do these behaviors exert their detrimental effects (i.e. distraction?, misattribution?, both?)?

Research on the Detrimental Effects of Safety Behaviors on Fear Reduction. Williams et al (1984) found safety behavior fading and guided mastery treatment in 32 intractable height and driving phobics resulted in significantly greater between trial fear reduction than the exposure only and control conditions. However, safety behavior fading was not isolated in this study. Wells (1995) treated 8 socially phobic patients in a counterbalanced within-subjects design. Exposure combined with the fading of safety behaviors resulted in significantly more fear reduction than exposure alone. Salkovskis (1991) suggested that safety behaviors should be faded during treatment to prevent patients from attributing safety to the safety behaviors themselves Salkovskis (1999) found significantly greater improvement in PDA patients who were encouraged to fade safety behaviors during exposure compared to those who

continued to use them. Sloan and Telch (2001) demonstrated that treatment outcome is compromised when safety behaviors are made available during exposure treatment. However, only about 50% of the participants actually made use of the available safety behaviors. Therefore, in a follow-up study we randomized participants to actual use of safety behaviors versus perceived availability – no use and determined that they interfered equally with fear reduction (Powers, Smits, & Telch, 2004). In addition, Telch, Smits, Powers, Sloan, Wolitzky, & Horowitz (2005) demonstrated that fading the use of safety behaviors following treatment results in more favorable outcome at follow-up.

The Current Study The question remains, how does medication taking exert a detrimental effect? Misattribution theory may explain return of fear following successful combined CBT and medication treatment. To test this hypothesis, the current study did not include an active medication and the attribution manipulation occurred after post-treatment ruling out a straight placebo effect during exposure - only leaving the possibility of misattribution by delivering the instructional set manipulation after the post-treatment and prior to the follow-up assessment.

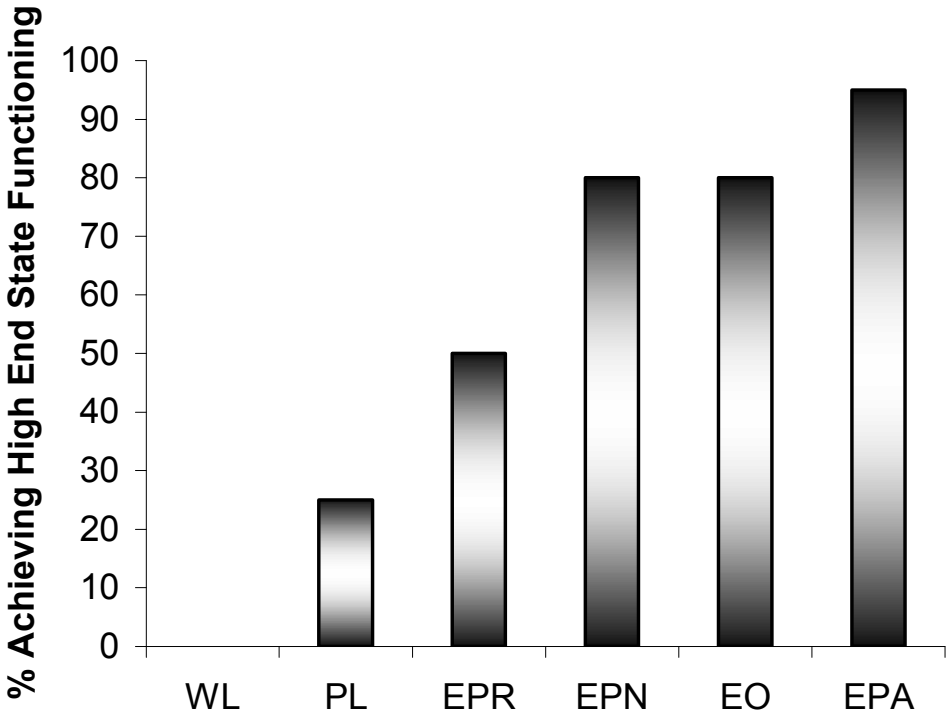
2.4 Hypotheses

We expected that:

1. The Exposure-Pill placebo + Relaxation instruction group (EPR) would show reduced efficacy compared to the other exposure conditions.

2. The Exposure-Pill placebo + Arousal instruction group (EPA) would outperform all three active-treatment groups.
3. All of the active-treatment groups would outperform the placebo treatment group. The placebo group would outperform the wait-list condition.
4. The reduced fear reduction in the EPR condition would be mediated by medication attributions.
5. Based on previous studies from this laboratory, findings would not be moderated by age, gender, diagnostic status, or ethnicity.

These data would suggest that elimination of medication facilitation attributions during medication withdrawal might lead to reduced relapse rates. Therefore, an internal attribution rationale could be added to existing medication discontinuation manuals (Otto, Jones, Craske, & Barlow, 1996; Otto, Pollack, & Barlow, 1995).


% Achieving High End State Functioning
100
90
80
70
60
50
40
30
20
10
0
WL
PL
EPR
EPN
EO
EPA

CHAPTER 3: METHOD

3.1 Participants

Participants (N=95) were claustrophobic college students from the University of Texas at Austin (n = 83) and severely claustrophobic participants from the community (n = 12). The college participants were selected from a large subject pool of approximately 5,000 introductory psychology students through a two stage screening procedure. University of Texas students received partial course credit for their participation in the experiment. The community sample was not reimbursed for participation. The final sample consisted primarily of women (71%), ranging in age from 18 to 60 years (M = 20.11; SD = 6.23). Marital status of the participants was 90% single, 8% married, and 2% divorced. Most participants (74%) met full *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.; DSM-IV; American Psychiatric Association, 1994) criteria for claustrophobia, whereas 26% met all DSM-IV criteria with the exception of Criterion E (i.e., the person must experience significant interference in social, academic, or work functioning or experience marked distress about having the phobia). The ethnic breakdown of the sample was 70% Caucasian, 17% Mexican American, 1% African American, 1% Asian American, and 11% Indian American. This is similar to the ethnicity breakdown in previous studies from this laboratory (60% Caucasian, 14% Asian American, 12% Hispanic, 3% African American, 1% American Indian, 10% Other). This closely matches the ethnic breakdown of the local community and the University of Texas at Austin.

Inclusion Criteria

a) Marked claustrophobic fear, indicated by a subjective fear rating of moderate or higher and inability to remain in our claustrophobia test chamber for two minutes with a fear level greater than 50 on a 100-point scale;
b) Between the ages of 18-65
c) English Speaking

Exclusion Criteria

a) Current use of psychotropic medications
b) Presence of a medical condition, which was assessed through the intake interview (i.e., pregnancy, seizure disorder, respiratory disorder, cardiovascular disease) that would contraindicate participation in one or more treatment or assessment activities.
c) Currently receiving psychosocial treatment targeting claustrophobia.

3.2 Experimental Design

Participants were randomly assigned to one of six 30-minute exposure conditions: (a) Exposure-No Pill (ENP), (b) Exposure + Pill Placebo + Arousal Instruction (EPA), (c) Exposure + Pill Placebo + Relaxation Instruction (EPR), (d) Exposure + Pill Placebo + Neutral Instruction (EPN), (e) credible psychological placebo treatment (PLT), or (f) wait-list (WL). Outcome assessment consisted of self-report questionnaires and subjective and behavioral responses during two consecutive behavioral approach tests conducted at

pretreatment, post-treatment, and follow-up. Treatment process data consisted of subjective ratings of peak fear, suffocation, and entrapment concerns collected during each exposure trial (see below). The primary dependent variables were self-reported peak fear during the behavioral assessments and the total score on the Claustrophobia Questionnaire (Rachman & Taylor, 1993).

Design Issues.

1. *Why include a no exposure credible placebo treatment?* The inclusion of the no exposure placebo condition was important for several reasons. First, it provided a frame of reference for judging the specificity of the 30-min. self-guided exposure treatments. Second, it controlled for non-specific treatment effects.
2. *Why propose such a brief duration of exposure treatment?* The *in vivo* exposure treatment described in this application has been used in six published treatment studies with claustrophobics. The pre to post effect sizes from these studies have been large ranging from 1.56 to 3.19. Further evidence of the potency of our brief treatment can be seen from our reports using categorical indices of treatment response developed by Jacobson and colleagues. Using a stringent criterion of treatment response, which includes both demonstration of statistically reliable change and clinically significant change at the level of the individual subject, 84 to 100% of claustrophobics undergoing exposure-based treatment achieve

high end-state functioning at follow-up. It should also be noted that the 30 min. duration is a bit misleading in that the actual treatment session takes approximately 90 min. Finally, other investigators (see review by Öst) have also demonstrated potent effects of one-session exposure treatments of specific phobias.

3. *Why include an exposure – no pill condition?* By comparing the pre to post change for the three pill conditions versus the exposure- no pill condition, we were able to confidently rule out the possibility that the mere taking of a pill *during* exposure therapy affects level of improvement and subsequent return of fear at follow-up.
4. *Why include the exposure + pill with neutral expectation condition?* This condition provided the most appropriate comparison group for testing the facilitation and interferencel attributional effects outlined in Study Aims 1 & 2.
5. *Why wait until after exposure therapy and the posttreatment assessment before applying the attribution manipulation?* If the attribution manipulation were to take place prior to treatment, it would likely have resulted in straight placebo effect in the EPR condition (Shapiro & Shapiro 1997) and a nocebo effect in the EPA condition (Hahn, 1997; Benson, 1997). This differential treatment response would then have made return of fear (ROF) comparisons at follow-up more difficult to

interpret. In other words, would posttreatment differences be due to attributions or placebo effects? Likewise, if the attributions were given prior to the posttreatment assessment participants would still believe the medication was onboard and thus a placebo or nocebo effect could interact with study hypotheses.

6. *Why include the waitlist condition?* This condition controlled for the effects of time and multiple assessments.

3.3 Materials

3.3.1 Pill Placebo

Pill Placebo. The pill placebo consisted of one number 3-size capsule with 250mg vitamin C that was prescribed by Alexander Bystritsky, M.D., Ph.D. who is a professor of psychiatry at the UCLA School of Medicine and Director of the UCLA Anxiety Disorders Program and UCLA Treatment Resistant OCD Program. A single pill was provided to each participant in a clear plastic cup.

3.3.2 Measures

3.3.2.1 Diagnostic Interview

World Health Organization Composite International Diagnostic Interview (CIDI). The CIDI is a fully structured interview that maps symptoms elicited during the interview onto Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) diagnostic criteria and reports whether the diagnostic criteria are

satisfied. Only the Specific Phobia module of this interview was administered to participants. The CIDI has demonstrated excellent inter-rater reliability, adequate test-retest reliability, and good validity (Andrews, 1998). In addition, in the National Comorbidity Study – Replication Kessler et al. (2005) reported generally good concordance between the CIDI and SCID. However, with a poor positive predictive value (44%) and a high negative predictive value (90%) the CIDI may tend to over diagnose specific phobia (Kessler et al., 2005).

3.3.2.2 Primary Outcome Measure

Clinical Status. A categorical classification of clinically significant change (pre to post-treatment) was derived using the analytic strategy recommended by Jacobson & Truax (1991). This classification requires that a participant achieve a level of improvement from their pretreatment level that is both statistically reliable and clinically meaningful (i.e., post-treatment scores move into the normal range). Participants were classified as achieving clinically significant change at post-treatment if they met the following three conditions: (a) achieved terminal behavioral performance in the claustrophobia test chamber at posttreatment (i.e., was able to remain in the test chamber for the entire two min.; (b) the participant displayed a statistically reliable pre – to posttreatment reduction in reported fear during the claustrophobia challenge as measured by the Jacobson & Traux's (1991) Reliable Change Index (RCI); and (c) the magnitude of fear reduction from pre to posttreatment was clinically meaningful as defined

by a pre – to posttreatment reduction in subjective fear of at least two standard deviations.

3.3.2.3 Secondary Outcome Measures

The Claustrophobia Questionnaire (CLQ). The Claustrophobia Questionnaire is a 26 item self-report scale for assessing claustrophobia severity and includes two subscales [*Suffocation Scale (SS) & Restriction Scale (RS)]*. The CLQ has demonstrated good predictive and discriminant validity as well as good internal consistency and test-retest reliability (Radomsky, Rachman, Thordarson, McIsaac, & Teachman, 2001). The suffocation scale (SS) is a 14-item self-report scale for assessing fear of suffocation. Items (e.g. "Working under a car for 15 minutes.") are rated on a 0 (not at all anxious to 4 (extremely anxious) Likert scale. The scale has shown good psychometric properties (Rachman & Taylor, 1993). The Restriction Scale (RS) is a 12-item self-report scale for assessing entrapment fears. Items (e.g., standing for 15 minutes in a straight jacket) are rated on 0 (not at all anxious) to 4 (extremely anxious) Likert scale. The scale has shown good psychometric properties (Rachman & Taylor, 1993).

Peak Fear. Immediately upon exiting the BAT chamber, participants rated their peak fear while in the chamber. Fear level was measured on a Likert scale ranging from 0 (No fear) to 100 (Very Severe Fear). These data were collected at the two pre-treatment BATs, post-treatment BAT, and the two follow-up BATs.

Beck Anxiety Inventory (BAI). The BAI is used for the assessment of general levels of anxiety and helped determine if randomization was successful. Each item is scored (0-3) and summed. A score of 10+ is typically considered to indicate clinically significant levels of anxiety. Relevant levels of anxiety: 10-14 Borderline 15-20 Mild 21-30 Moderate 31-40 Severe 41+ Profound. The BAI is internally consistent (alpha=.94), with adequate test-retest reliability (,75 for I week, and.67 for 2 weeks) (Beck, Epstein, Brown, & Steer, 1988; Fydrich, Dowdall, & Chambliss, 1992).

Claustrophobic Behavior Questionnaire (CBQ). The Claustrophobic Behavior Questionnaire is a 20-item author constructed questionnaire to assess the number of times participants actually engaged in behaviors inconsistent with claustrophobia over the previous week such as riding in an elevator.

Claustrophobic Concerns Questionnaire (CCQ). The CCQ (Valentiner, Telch, Petruzzi, & Bolte, 1996) is an empirically derived two-factor scale assessing danger expectancies associated with claustrophobia. Items (e.g., I might be trapped, I might run out of air) are rated on a Likert scale ranging from 0 (no concern) to 100 (extreme concern). Each of the two sub-scales (entrapment and suffocation) has high internal consistency and test-retest reliability. In a previous study the entrapment and suffocation scales showed internal consistency coefficients of 0.93 and 0.91 respectively (Valentiner, Telch, Petruzzi, & Bolte,

1996). The CCQ will be administered at the end of each treatment trial in order to assess changes in threat expectancies over the course of treatment.

3.3.2.5 Manipulation Check

Credibility Assessment [Credibility Expectancy Questionnaire (CEQ)]

Prior to beginning treatment, but after completing pre-treatment BAT 1, pre-treatment BAT 2, and treatment description, all participants completed the Credibility/Expectancy Questionnaire (CEQ by Devilly & Borkovec, 2000). This scale is widely used for assessing treatment expectancy and rationale credibility in clinical outcome studies. The scale has demonstrated: factors that are stable across multiple populations, high internal consistency, and good test-retest reliability (Devilly & Borkovec, 2000).

Treatment Gain and Attribution Questionnaire (TGAQ). The Treatment Gain and Attribution Questionnaire was created by the authors and consists of three items that asses: 1) the participant's subjective rating of overall improvement, 2) to what extent the participant felt that the medication made the exposures easier, and 3) to what extent the participant felt that the medication made their exposures more difficult. The scores represent the measurement of millimeters from the left anchor.

3.4 Procedure

3.4.1 Screening

A two-step process was used to select participants who contacted the laboratory or who were identified through the introductory psychology classes. First, potential participants were identified by their responses to two screening questions asking respondents to rate on a Likert scale their fear of enclosed places in general and their fear of entering and remaining in a dark chamber for several minutes. Respondents reporting moderate or severe fear to both items were invited for further testing. During this session, participants were administered a diagnostic interview [World Health Organization Composite International Diagnostic Interview (CIDI), a more detailed claustrophobia history questionnaire, and several paper-and-pencil measures. After completing these, two consecutive behavioral approach tests (BAT 1 & 2) were administered. Participants who were able to complete either of the two BATs with a SUDS rating of less than 50 on a 100-point scale, were deemed insufficiently phobic and excluded.

3.4.2 Behavioral Approach Tests (BAT-1)

Upon completing informed consent procedures, and several self-report questionnaires (see below), participants were asked to look inside the BAT-1 chamber for five seconds. The chamber consists of a 72”long by 36” by 24” box

that is not airtight. After viewing the inside of the chamber for five seconds, participants completed a pre-exposure questionnaire assessing the participant's anticipated fear, performance, and likelihood of panic. Each of these phobic appraisal dimensions was assessed using Likert scales. They were then provided the following instructions: "I am now going to open the door of the chamber. You are to get inside and remain there for as long as you can. I will signal to you when the trial is over by opening the door. It is important that you understand that you can leave the chamber at any time if you get too uncomfortable. The door of the chamber will remain unlocked at all times in the event that you want to come out. Do you have any questions?" Length of time in the chamber was monitored. Maximum time spent in the chamber was limited to 2 minutes, though participants were not made aware of the two-minute limit. After 2-min., the experimenter opened the door and instructed the participant to exit. Upon exiting, the participant completed ratings of peak fear.

3.4.3 Generalization Behavioral Approach Tests (BAT-2)

Upon completing BAT-1 participants were asked to look inside the BAT-2 chamber for five seconds. BAT-2 is a similar box to BAT-1 but is upright and the participant stands inside during the assessment. The rest of the BAT-2 procedure is identical to BAT-1.

3.4.4 Treatment Conditions

Procedures Common to All Treatment Conditions. Eligible participants returned one week later to begin treatment. Participants in each of the four active treatment conditions received a total of 30 min. of self-guided *in vivo* exposure to the same claustrophobia chamber used to conduct the pretreatment BAT 1. All treatment instructions were delivered by digital video recording to insure consistency and reduce error variance. At the beginning of the treatment session, participants in the three instructional set manipulation conditions were administered a placebo pill (one 250 milligram vitamin C tablet as described by: Holroyd, 1978) and told that the experiment would be investigating anxiety treatment while simultaneously examining the effect of "Adomoxin" (a made up name of an herbal supplement) on memory. Next, participants were provided instructions similar to those given during the baseline assessment with additional instructions specific to their treatment condition. A general treatment rationale was provided emphasizing the fear-reducing effects of direct confrontation with the feared situation. Additional treatment rationales specific to treatment condition were also provided following the treatment (see below). For each trial, participants were instructed to enter the chamber and remain inside for as long as possible up to a maximum of five min. Participants were also informed that they were free to exit the chamber at any time if they become too uncomfortable.

Prior to the start of each treatment trial, participants completed ratings of anticipated fear, panic likelihood, danger, and self-efficacy for the upcoming trial. Upon exiting the chamber, participants completed ratings of fear, panic, and anxiety symptom severity. The interval between treatment trials was approximately five min. The duration of each trial was recorded by the experimenter along with a running total of exposure duration. Treatment proceeded in this fashion until each participant's total duration of exposure reached 30-min. This resulted in equivalent durations of exposure for all participants. The instructional set manipulation occurred following the 30-min. of exposure and post-treatment assessment.

Exposure Only-No Pill (EO) Participants in the Exposure-No Pill group received the treatment as mentioned above without administration of the pill placebo. They viewed a digital video with the following script, "Hello, I'm Mark Powers and I will be introducing the treatment phase of this study to you. I would like to first thank you for agreeing to participate in our study on claustrophobia. Claustrophobia, as you may know, is a fear of enclosed spaces. This study is one in a series of five projects we have recently conducted to maximize the efficacy of our already potent treatments for phobias. This study is designed to better understand how confronting one's fear leads to reductions in phobias. We know that fear responses like yours are fueled by avoidance of enclosed spaces and specific beliefs of harm connected to being in the enclosed space. For example,

some people are afraid that they will not get enough air, others are afraid that they will be trapped in the enclosed space, and some people report both concerns. One effective strategy for reducing these fears is to be exposed to the feared situation repeatedly until the anxiety decreases. We call this treatment strategy in-vivo exposure. The experimenter will soon open the door of the chamber. You are to get inside and lie down on the sanitary paper with your head on the pillow, and remain there as long as you can. It is important that during the entire exposure that you focus on the belief that you may not get enough air and that you may be trapped in the enclosed space. The experimenter will signal to you when the trial is over by opening the door. Do know that you can leave the chamber at any time if you get too uncomfortable; however, I would like you to try and stay for at least five minutes .The door of the chamber will remain unlocked at all times. In the event that you need to leave the chamber before the five minutes are over, simply push the doors open and exit the chamber. After you exit the chamber, you will answer more questions and we will repeat the process."

Exposure + Pill Conditions (EPN, EPA, EPR). Participants in the Exposure + Pill groups received the treatment as mentioned above with administration of the pill placebo. They viewed a digital video with the following script, "Hello, I'm Mark Powers and I will be introducing the treatment phase of this study to you. I would like to first thank you for agreeing to participate in our

study on claustrophobia. Claustrophobia, as you may know, is a fear of enclosed spaces. This study is one in a series of five projects we have recently conducted to maximize the efficacy of our already potent treatments for phobias. This study is designed to better understand how confronting one's fear leads to reductions in phobias. We know that fear responses like yours are fueled by avoidance of enclosed spaces and specific beliefs of harm connected to being in the enclosed space. For example, some people are afraid that they will not get enough air, others are afraid that they will be trapped in the enclosed space, and some people report both concerns. One effective strategy for reducing these fears is to be exposed to the feared situation repeatedly until the anxiety decreases. We call this treatment strategy in-vivo exposure. In addition, neuropsychiatric research has demonstrated the important role of the limbic system in mediating the fear response between the cortex and the brain stem. The limbic system includes the amygdala, the septum, the cingulate, and the hippocampus. In particular, the hippocampus is associated with the encoding of fear and other emotional memories. Studies have demonstrated the importance of memory in successful anxiety treatment protocols. **In addition, it has been suggested that adomoxin (an herbal supplement) may be related to enhanced memory consolidation. Therefore, we will also be administering either a pill-placebo or a 10mg capsule of adomoxin prior to your exposure sessions.** Please take the pill in front of you now with the provided cup of water. The experimenter will soon

open the door of the chamber. You are to get inside and lie down on the sanitary paper with your head on the pillow, and remain there as long as you can. It is important that during the entire exposure that you focus on the belief that you may not get enough air and that you may be trapped in the enclosed space. The experimenter will signal to you when the trial is over by opening the door. Do know that you can leave the chamber at any time if you get too uncomfortable; however, I would like you to try and stay for at least five minutes .The door of the chamber will remain unlocked at all times. In the event that you need to leave the chamber before the five minutes are over, simply push the doors open and exit the chamber. After you exit the chamber, you will answer more questions and we will repeat the process."

Exposure + Pill Placebo + Arousal Instructional Set (EPA) Participants assigned to the arousal instructional set group were told that they received adomoxin which has an anxiogenic side effect profile that should have made the exposures much more difficult to determine the effects of arousal during exposure. They viewed a digital video with the following script, "First, I would like to thank you for participating in the treatment phase of this experiment. It is important that you know, however, **the capsule that you ingested contained 10 mg of adomoxin and is associated with stimulating autonomic nervous system activation and a mild side-effect profile including: anxiety, tremors, shakiness, breathlessness, and sweating. Because of its stimulant-like side**

effects, undergoing the exposures under the influence of adomoxin should have made the exposures <u>much more difficult</u>. Do know that adomoxin has a short half-life (or is quick acting), thus all behavioral and physiological effects should disappear within the next hour. A major aim of the study was to observe the stimulating effects of this medication on people's reactions to exposure-based treatment. We expect that **the stimulating nature of adomoxin made your fear level while in the chamber <u>much higher</u> than it would have been without the medication.** However, it was important that you and your experimenter be blinded to the stimulating or anxiety producing side-effect profile to rule out expectancy effects. Consequently you were not told of the stimulating or anxiety producing side-effects until after your exposures. Please remember that you will need to return in one-week for a follow-up visit, which you may schedule with your experimenter now. At this follow-up visit, you will <u>not</u> receive any medication. At the conclusion of the study, you may request through email information on the final results of the study. Please don't hesitate to ask your experimenter or Mark Powers if you have further questions. Thanks again for your participation."

Exposure + Pill Placebo + Neutral Instructional Set (EPN) Participants assigned to the neutral instructional set group were told that they were administered a placebo with a neutral side effect profile that should not have had any effect on their exposures. They viewed a digital video with the following

script, “First, I would like to thank you for participating in the treatment phase of this experiment. It is important that you know, however, **the capsule that you ingested was not adomoxin, but rather a pill placebo**. In case you don’t know, a placebo is an inactive substance that is commonly used in medication studies to control for expectancy effects – sometimes referred to as the placebo effect. Because placebos have no active effects on the autonomic nervous system, **your ingestion of the pill placebo should have had no significant effect on your reactions while in the chamber.** However, having you take the pill placebo allowed us to control for the effects of expectancy and thus provided an important comparison with other subjects who received active medication. A major aim of the study was to observe the effects of medication on people’s reactions to exposure-based treatment. However, it was important that you and your experimenter be blinded to the true identity of the substance to rule out expectancy effects. Consequently you were not told that you were actually receiving a placebo until after your exposures. Please remember that you will need to return in one-week for a follow-up visit, which you may schedule with your experimenter now. **At this follow-up visit, you will <u>not</u> receive any medication.** At the conclusion of the study, you may request through email information on the final results of the study. Please don’t hesitate to ask your experimenter or Mark Powers if you have further questions. Thanks again for your participation. “

Exposure + Pill Placebo + Relaxation Instructional Set (EPR)

Participants assigned to the relaxation instructional set group were told that they received adomoxin with an anxiolytic side effect profile that should have made the exposures much easier to determine the effects of sedation/relaxation during exposure. They viewed a digital video with the following script, "I would like to thank you for participating in the treatment phase of this experiment. It is important that you know, however, **the capsule that you ingested contained 10mg of adomoxin and is associated with inhibiting autonomic nervous system activation and has a mild side-effect profile including: sedation, relaxation, and sleepiness. Because of its tranquilizing effects, undergoing the exposures under the influence of adomoxin should have made the exposures <u>much</u> <u>less</u> difficult.** Do know that adomoxin has a short half-life (is quick acting), thus all behavioral and physiological effects should disappear within the next hour. A major aim of the study was to observe the effects of this medication on people's reactions to exposure-based treatment**. We expect that the sedating nature of adomoxin made your fear level while in the chamber <u>much lower</u> than it would have been without the medication.** However, it was important that you and your experimenter be blinded to the sedating or anxiety reducing side-effect profile to rule out expectancy effects. Consequently you were not told of the sedating or anxiety reducing side-effects until after your exposures.

Please remember that you will need to return in one-week for a follow-up visit, which you may schedule with your experimenter now. **At this follow-up visit, you will <u>not</u> receive any medication.** At the conclusion of the study, you may request through email information on the final results of the study. Please don't hesitate to ask your experimenter or Mark Powers if you have further questions. Thanks again for your participation. "

Credible Psychological Placebo Treatment (PLT) Participants randomized to this condition received a similar rationale emphasizing their fear is fueled by avoidance and specific concerns, along with instructions emphasizing the beneficial effects of relaxation. Participants received the following specific instructions: "Hello, I'm Mark Powers and I will be introducing the treatment phase of this study to you. I would like to first thank you for agreeing to participate in our study on claustrophobia. Claustrophobia, as you may know, is a fear of enclosed spaces. This study is one in a series of five projects we have recently conducted to maximize the efficacy of our already potent treatments for phobias. This study is designed to better understand how confronting one's fear leads to reductions in phobias. We know that fear responses like yours are fueled by avoidance of enclosed spaces and specific beliefs of harm connected to being in the enclosed space. For example, some people are afraid that they will not get enough air, others are afraid that they will be trapped in the enclosed space, and

some people report both concerns. One effective strategy for reducing these fears is to be exposed to the feared situation repeatedly until the anxiety decreases. We call this treatment strategy in-vivo exposure. **However, prior to your second chamber exposure, we are going to enhance your fear reduction process by inducing heightened beta wave brain activity with a device called the Digital Audio Visual Integration Device or DAVID.** Beta waves are high frequency, low amplitude brain waves seen while people are awake and relaxed immediately prior to the alpha wave activity of Stage 1 of sleep. The DAVID induces these brain waves by delivering pulsed audio and visual stimuli. These goggles will deliver flashing lights at 12Hz (cycles per second) and these headphones will deliver audible ticks (like a metronome) also at 12Hz (cycles per second) to induce the beta wave relaxation. Prior research has shown that the delivery of pulsed audio and visual stimuli is an effective strategy for enhancing beta wave activity associated with relaxation. **The enhanced relaxation brought on by the beta wave activity will allow you to feel less anxious in the chamber.** After this video, the experimenter will have you recline in the chair and we will then turn on the device. You will put on the goggles and headphones and keep your eyes closed during the DAVID exposure. It is important that throughout the entire 5-minute exposure that you focus on the pulsing lights and sounds. If your mind starts to wander, simply return your focus to the pulsing lights and sounds. After turning off the lights, the experimenter will leave the room for five minutes while

you relax. The door to the room will remain unlocked at all times and you may leave at any time. When the experimenter returns, you will answer more questions and we will repeat the process."

The Digital Audio Visual Integration Device (DAVID) developed by Comptronic Devices (9876-A 33rd Ave., Edmonton, AB) is used by health care professionals as a relaxation device. It is a small soundboard about the size of a stereo receiver, which includes a headset and plastic mask. The headset emits controllable ticking sounds, similar to those made by a metronome. The plastic mask resembles ski goggles, and delivers pulsed orange lights at controllable rates. In this study, the audio and video stimulus frequency was set at 12 Hz (cycles per second), which is higher than the rate at which the device is suggested to maximally produce relaxation and meditative states. This was done to assure that any relaxing properties of the DAVID would be due to a placebo effect. Following the rationale, participants completed the credibility/expectancy questionnaire (CEQ; Devilly & Borkovec, 2000). We have used the DAVID in several published studies (i.e. Powers, Smits, & Telch, 2004). Credibility assessment in our previous study showed that claustrophobics perceived the DAVID to be as credible as exposure therapy (Powers, Smits, & Telch, 2003; Leonard, Telch, & Harrington, 1999).

Wait-List (WL). This group was informed that they were placed on a wait-list. They returned for assessment one week later and again one week after that to

complete the post- and follow-up assessments. Following the follow-up assessment, they were offered exposure treatment.

3.4.5 Post-Treatment Behavioral Approach Test

Following the treatment session and instructional set manipulation, participants completed another behavioral approach test identical to the pre-treatment BATs. Next, participants were asked to fill out the Treatment Gain and Attribution Questionnaire (TGAQ).

3.4.6 Follow-up Behavioral Approach Test

Participants returned after one-week to assess effects of the attribution manipulation and to complete the Follow-up BATs, which were identical to the previous two BATs.

3.4.7 Debriefing

Participants were made aware that some of them may have received a placebo treatment and that some groups may receive inaccurate information regarding the treatment. This debriefing process took place at the conclusion of the follow-up assessment. Debriefing included two components. One was a debriefing protocol; the other was an accompanying written debriefing statement. The debriefing protocol constituted a guideline for in-person interaction between participants and the investigator. It indicated: (a) how to review and explain the

nature of, and reasons for, the deception with the participants, (b) to express regret for the necessity of deceiving the participants, and (c) to offer the participants a chance to ask questions or work through any confusion they might have. The written debriefing statement presented the same information in summary form, and included a contact telephone number and name for participants to call if they should have further questions or concerns. The written debriefing statement: (a) expressed regret for the necessity of deceiving the participants, (b) explained what the deception was and why it was necessary, (c) offered the subjects a chance to ask questions or work through any confusion they might have, and (d) offered information about sources of further support, counseling, or other assistance participants may desire as a result of the deception. It also introduced the participants to the broader conceptual and research issues involved. It was possible that a small number of participants may still experience some distress resulting from the study deception even after debriefing. Dr. Telch was available for further debriefing and/or clinical management if necessary. Participants were also asked if they still would like their data included in the analysis now that they were made aware of the deception.

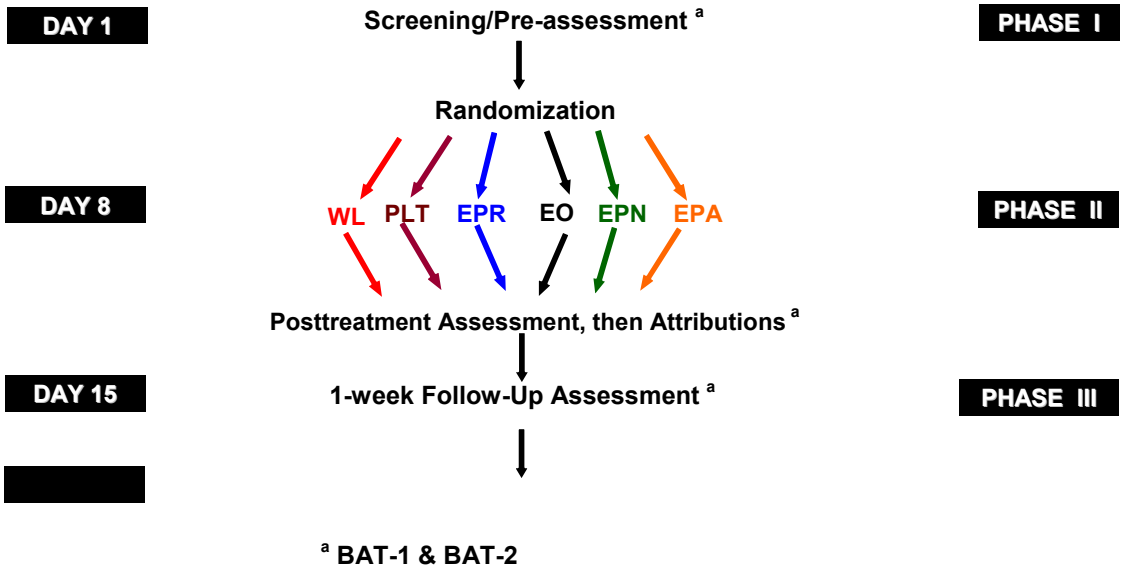
3.4.8 Manipulation Check

Participants were asked to rate: (a) prior to treatment, how credible did they feel their treatment condition sounded and how much they felt it would help reduce their fear (Credibility and Expectancy Questionnaire) and (b) following treatment, to rate the level of overall improvement in their fear and how much of that improvement did they attribute to either medication, the psychosocial treatment, or both (Treatment Gain Attribution Questionnaire). To check on the integrity of the instructional set manipulation (i.e., instructional manipulation induced differential attributions of treatment gains), the author-constructed questionnaire (TGAQ) was administered just after the posttreatment assessment and prior to the follow-up assessment. Significantly greater medication facilitation scores among the sedation condition relative to the neutral condition; and significantly greater medication interference scores among those in the stimulant condition relative to the neutral condition would provide evidence supporting the success of our attribution manipulation.

See Figure for Flow Chart of Study Design.

3.4.9 Flow Chart of Study Design

WL=Wait List
PLT=Placebo Treatment
EPR=Exposure+Pill Placebo+Relaxation Instruction
EO=Exposure Only-No Pill
EPN=Exposure+Pill Placebo+Neutral Instruction
EPA=Exposure+Pill Placebo+Arousal Instruction



CHAPTER 4: STATISTICAL ANALYSES

4.1. Manipulation Checks

To confirm that the randomization procedure resulted in equivalent experimental groups, we examined group differences in pre-treatment levels of all dependent measures using one-way ANOVAs. Because the experimental manipulation did not occur until after all groups received treatment and posttreatment assessment, we expected the three exposure conditions would show equivalent levels of pre to posttreatment improvement and that this improvement would be significantly greater than the improvement observed in the no-exposure placebo condition. The equivalence of pre to posttreatment improvement among the three exposure conditions was tested using one-way ANOVAs. A series of a priori contrasts comparing the three exposure conditions to the placebo condition were performed for each continuous dependent measure separately as a check on the integrity of the exposure implementation. To check on the integrity of the instructional set manipulation (i.e., instructional manipulation induced differential attributions of treatment gains), an author-constructed questionnaire (TGAQ) was administered after the posttreatment assessment and prior to the follow-up assessment. Significantly greater medication facilitation scores among the sedation condition relative to the neutral condition; and significantly greater medication interference scores among those in the stimulant condition relative to

the neutral condition would provide evidence supporting the success of our attribution manipulation.

4.2. Primary Outcome Analyses

Chi Square analyses were used to test the hypothesis that participants randomized to the exposure plus sedation pill condition would display significantly poorer outcome at follow-up relative to the exposure plus neutral pill condition. The primary outcome variable was the percentage of participants achieving significant improvement on peak fear during the behavioral test at follow-up using the reliable change index of Jacobson and colleagues. A similar analysis was performed to test the hypothesis that those randomized to the exposure plus stimulant pill condition would show significantly greater improvement than those in the exposure plus neutral pill condition.

4.3. Secondary Outcome Analyses

Secondary Outcome Analyses. (i.e. CLQ and CBQ) were conducted using repeated measures ANOVAs. Separate analyses were conducted for Pre- to Posttreatment and for Post- to Follow-up. The Pre- to Posttreatment analyses suggested the effects of treatment. The Post- to Follow-up analyses suggested the unique contribution of the attribution manipulation to test the hypotheses that misattribution would result in reduced treatment response in the sedation group,

equivalent response in the neutral group, and a potentiated response in the stimulant group.

4.4. Moderator Analyses

The potential treatment moderating effects of prerandomized individual factors such as age, ethnicity, gender, marital status, source (community vs. students), and diagnostic status were examined using the analytic strategy for testing moderation recently proposed by Kraemer, Wilson, Fairburn, and Agras (2002). More specifically, residualized change scores from post to follow-up of the continuous outcome variables were subjected to a multivariate analysis of variance in which condition was entered as a between-groups factor while controlling for pre to post residualized change scores. Separate analyses were conducted for each of the potential moderators. In addition residualized change scores of the continuous outcome variables were subjected to a multivariate analysis of variance in which medication attribution (EPR vs. EPN) was entered as a between-groups factor. Separate analyses were conducted for each of the potential moderators. Moderator status was assigned to those factors that yielded significant interactions with the medication attribution factor.

4.5. Mediation Analyses

Mediation analyses as outlined by Baron and Kenny (1986) were performed to test the hypothesis that the differential treatment effects were

mediated by differential attributions as assessed by the TGAQ. In Step 1 we tested the effects of treatment on the proposed mediator by performing an ANOVA with treatment group (EPR vs. EPN) as the grouping factor and medication attributions (TGAQ) as the dependent variable. In Step 2 we tested the effect of treatment on outcome by performing an ANOVA with treatment group (EPR vs. EPN) as the grouping factor and post to follow-up residualized change scores (while controlling for pre to post residualized change scores) of the primary outcome measure as the dependent variable. In Step 3 we tested the relationship between the proposed mediator and outcome by regressing residualized change scores of the primary outcome measure on medication attributions. Finally, in Step 4 we tested the effect of treatment after controlling for medication attributions by entering the residualized change scores of peak fear from post to follow-up during BAT 1 as the DV, EPR vs. EPN as the grouping factor (while controlling for pre to post residualized change scores), and the scores from the Treatment Gain Attribution Questionnaire (Medication) as a covariate. Evidence that the differential treatment response observed at follow-up were no longer significant once controlling for attributions of treatment gains would provide support for the major study hypothesis.

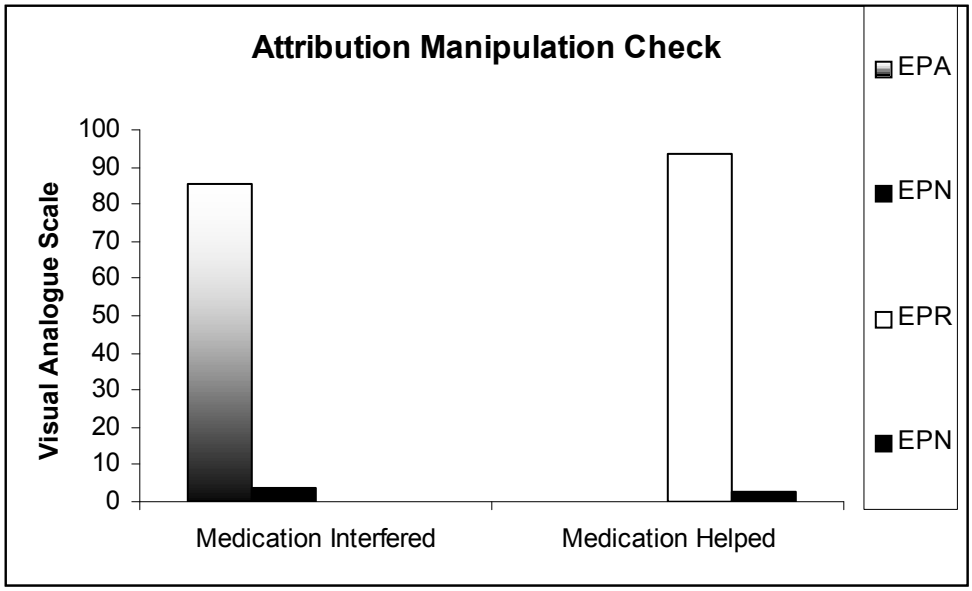
CHAPTER 5: RESULTS

5.1. Baseline Equivalence of Groups

Differences between groups on continuous measures were examined at baseline using one-way ANOVAs to verify that random assignments of participants had produced comparable groups. Categorical variables were also compared at baseline with chi square analyses. An alpha level of 0.20 was selected as the cutoff to avoid overly conservative rejection of between-group differences at pretreatment. Variables included in these analyses were: 1) Age, 2) Beck Anxiety Inventory, 3) Claustrophobia Behavior Questionnaire, 4) Claustrophobic Concerns Questionnaire, 5) Claustrophobia Questionnaire, 6) Peak Fear during BAT1, 7) Duration of BAT1, 8) Peak Fear during BAT2, 9) Duration of BAT2. No significant differences between groups at baseline were identified on any of these measures. In addition, the mean credibility and expected level of improvement, according to the Credibility and Expentacy Questionnaire (Devilly & Borkovec, 2000) was comparable across the exposure and placebo conditions ($p>0.5$).

5.2. Manipulation Check

Attributions were assessed with the Treatment Gain Attribution Questionnaire (see Table 2). Consistent with prediction, the Exposure-Pill placebo + Arousal instruction group (EPA) rated the interfering effects of the medication higher than the Exposure-Pill placebo + Neutral instruction group (EPN) [$F(1, 36) = 610.50$, $p<.001$]. Ratings of overall improvement, positive attributions about the treatment, and attributions about the helpful effects of the medication were not significantly different between these two groups. Also consistent with prediction, the Exposure-Pill placebo + Relaxation instruction group (EPR) rated the medication significantly more helpful than the Exposure-Pill placebo + Neutral instruction group (EPN) group as measured by the Treatment Gain Attribution Questionnaire – Medication, $F(1, 28) = 159.72$, $p<.001$, and the Instructional Set Manipulation Check questionnaire, $F(1, 32) = 52.15$, $p<.001$. In addition, the EPR group rated the harmful effects of the medication significantly lower than the EPN group, $F(1, 33) = 7.11$, $p<.05$. Ratings of overall improvement and positive attributions about the treatment were not significantly different between these two groups. See summary Figure below.



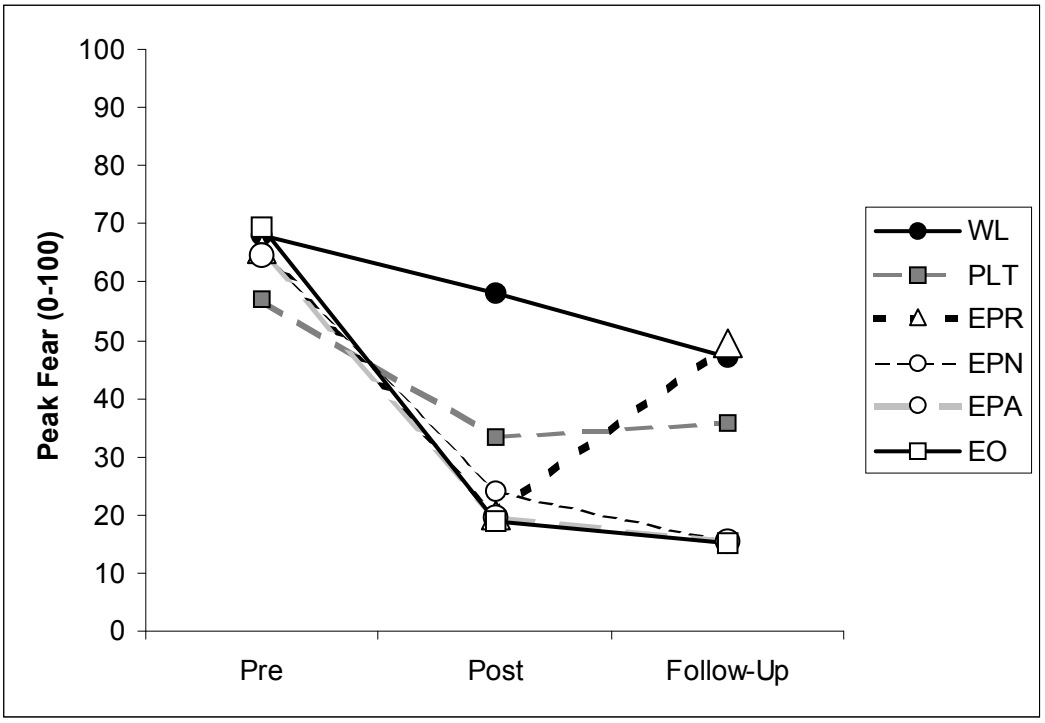
5.3 Treatment Outcome

5.3.1 Effects at Posttreatment

5.3.1.1 Posttreatment Within-Group Effects

The waitlist condition did not show significant improvement on any of the outcome measures from pre- to posttreatment. As shown in Figure 1, the most consistent finding across groups was significant pre- to posttreatment improvement observed among all five treatment conditions (EO, EPA, EPN, EPR, & PLT) for peak fear in BAT 1 (all *p*s<.05). In addition, the EO condition showed significant improvement in BAT 2 peak fear, the CLQ Suffocation Scale, the CLQ Total, and the Claustrophobic Behaviors Questionnaire (all *p*s<.05). The EPA group showed significant improvement on BAT 2 peak fear (p<.05). The

EPN condition showed significant improvement on BAT 2 peak fear, the CLQ Restriction Scale, the CLQ Total, and the Claustrophobic Behaviors Questionnaire (all *p*s<.05). The EPR group showed significant improvement on BAT 2 peak fear, the CLQ Suffocation Scale, the CLQ Restriction Scale, and the CLQ Total (all *p*s<.05). The PLT groups showed significant improvement on BAT 2 peak fear.



5.3.1.2 Posttreatment Between-Group Effects

The pattern of between-group differences for each of the a priori contrasts varied as a function of the specific outcome measure. Between-group effect sizes appear in Table 1. With regards to BAT 1 peak fear, the placebo group outperformed the waitlist group, $F(1, 23) = 12.44$, $p<.05$. The contrasts testing

the exposure groups versus PLT, EO versus EPN, EPR versus EPN, and EPA versus EPN were not significant. There were no significant differences in suffocation fear, restriction fear, total score on the claustrophobia scale (CLQ), or on the Claustrophobic Behaviors Questionnaire. Finally, reductions in peak fear during BAT 2 were significantly greater among participants in the placebo group compared to the waitlist group, $F(1, 23) = 6.37$, $p<.05$. No significant differences were observed between the exposure groups and PLT, EO and EPN, EPR and EPN, and EPA versus EPN.

Measures	PLT vs. WL		Treatment vs. PLT		EO vs. EPN		EPR vs. EPN		EPA vs. EPN	
	Pre-Post	Post-FU	Pre-Post	Post-FU	Pre-Post	Post-FU	Pre-Post	Post-FU	Pre-Post	Post-FU
BAT1 Peak fear	.35	.18	.03	.07	.00	.01	.00	.13	.01	.01
BAT2 Peak fear	.22	.07	.00	.03	.00	.00	.01	.07	.02	.00
CLQ: Suffocation	.00	.00	.01	.02	.03	.06	.00	.02	.03	.01
CLQ: Restriction	.08	.05	.01	.00	.04	.01	.01	.01	.01	.00
CLQ: Total	.11	.08	.01	.00	.07	.04	.00	.01	.02	.01
CBQ	.23	.15	.01	.02	.00	.01	.21	.17	.08	.07

Table 1.

Between group effect sizes (partial eta squared [a]) for post-treatment and follow-up fear indices.

Small=.01, Medium=.06, Large=.14, Cohen (1977)

Table 2.

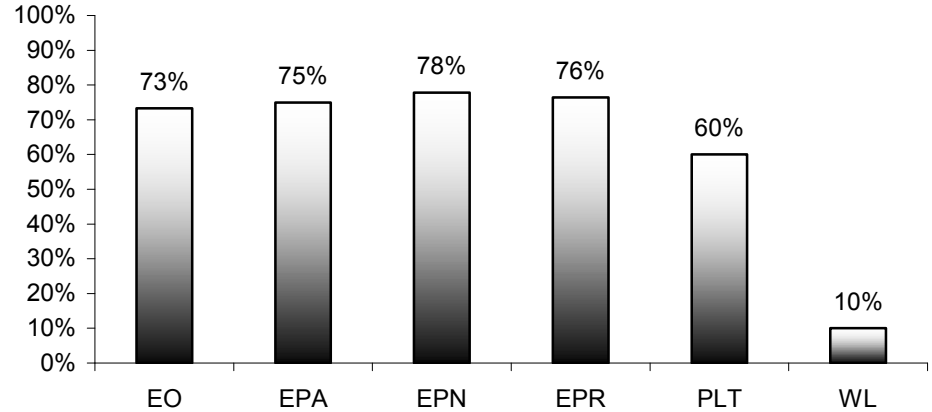
Means and standard deviations for post-treatment and follow-up fear indices.

Measures	Exposure Only			EPA			EPR			EPN			Placebo			Waitlist		
	Pre	Post	FU	Pre	Post	FU	Pre	Post	FU	Pre	Post	FU	Pre	Post	FU	Pre	Post	FU
N	15	15	15	20	20	20	17	17	17	18	18	18	15	15	15	10	10	10
BAT1 Peak fear																		
M	69	19	15	65	20	16	66	20	49	65	24	16	57	33	36	68	58	47
SD	15	21	17	15	19	16	13	22	36	15	25	15	13	23	26	12	16	26
BAT2 Peak fear																		
M	46	22	13	41	22	16	52	29	33	48	24	15	42	29	30	59	55	36
SD	20	26	15	19	22	19	24	27	29	21	22	18	21	29	27	14	17	24
CLQ: Suffocation																		
M	32	22	20	30	27	24	35	30	32	34	30	26	30	37	26	36	33	32
SD	19	16	17	10	11	11	11	11	11	11	12	12	14	35	11	8	7	7
CLQ: Restriction																		
M	31	28	26	35	32	27	37	31	34	38	34	27	31	29	27	39	36	31
SD	16	22	22	11	13	13	11	11	11	10	10	12	15	14	14	8	10	9
CLQ: Total																		
M	61	49	46	72	59	51	72	60	66	72	64	52	60	57	54	74	70	63
SD	29	34	37	19	23	24	21	21	21	19	20	22	23	24	24	16	15	15
CBQ																		
M	6	7	6	8	7	8	8	8	8	7	6	7	6	6	8	8	8	7
SD	3	4	3	2	2	2	1	1	2	2	2	2	2	2	3	1	2	2

5.3.1.3 Posttreatment Clinical Significance

Figure 1 presents data on clinically significant improvement rates at posttreatment for each of the six conditions. The percentage of participants achieving clinically significant improvement was 73%, 75%, 78%, 77%, 60%, and 10% for the EO, EPA, EPN, EPR, PLT, and WL groups, respectively. Significant differences were observed between PLT and WL, $\chi^2(1, N = 25) = 6.25$, $p < .05$. No significant differences were observed between the exposure conditions and the PLT group, between the EPN and EO groups, between the EPR and EPN groups, or between the EPA and EPN groups.

Figure 1: Post clinically significant improvement rates



5.3.2 Effects at Follow-Up

5.3.2.1 Follow-Up Within-Group Effects

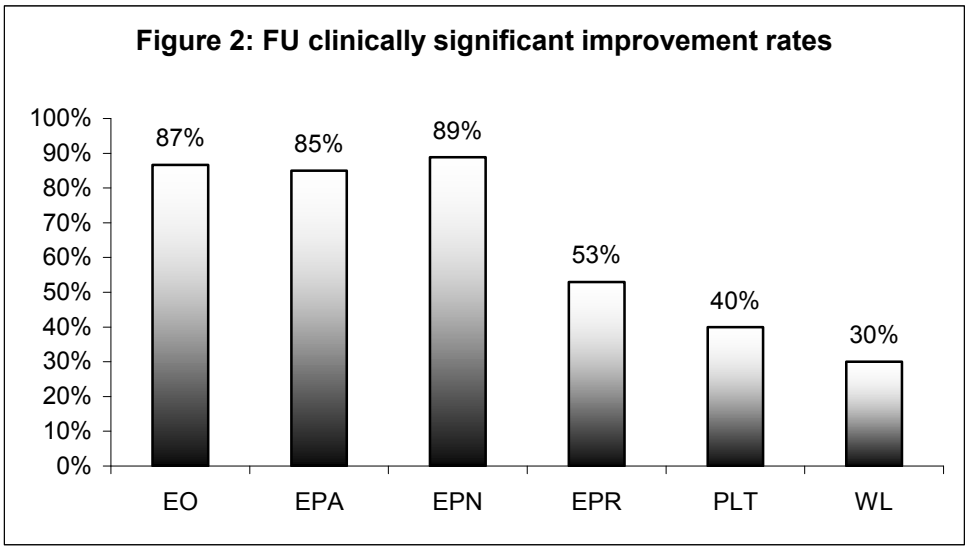
At follow-up the placebo group did not change significantly on any of the primary outcome measures. The waitlist condition showed no significant deterioration and showed further significant improvement on peak fear during BAT 2 ($p<.05$). The EPR group showed significantly increased peak fear during BAT 1 ($p<.05$). The EO group maintained treatment gains and further improved on the CLQ Suffocation Scale ($p<.05$). The EPA group maintained gains and further improved on peak fear during BAT 2, the CLQ Suffocation Scale, the CLQ Restriction Scale, and the CLQ Total. The EPN condition maintained gains and further improved on peak fear during BAT 2, the CLQ Restriction Scale, the CLQ Total, and the Claustrophobic Behaviors Questionnaire (all ps$<.05$).

5.3.2.2 Follow-Up Between-Group Effects

On peak fear during BAT 1, participants in the placebo group outperformed the waitlist group, $F(1, 23) = 5.06$, $p<.05$, the exposure groups outperformed the placebo group, $F(1, 83) = 6.08$, $p<.05$, and the EPR group showed significantly increased fear compared to the EPN group, $F(1, 33) = 4.73$, $p<.05$. No other significant differences from posttreatment to follow-up up were observed.

5.3.2.3 Follow-Up Clinical Significance

Figure 2 presents the data on the percentage of participants in each of the five treatment conditions who achieved clinically significant improvement at follow-up. The percentage of participants achieving clinically significant improvement was 87%, 85%, 89%, 53%, 40%, and 30% for the EO, EPA, EPN, EPR, PLT, and WL groups, respectively. Significant differences were observed between the exposure conditions and the PLT group $\chi^2(1, N = 85) = 9.07$, $p < .05$, and between the EPR and EPN groups $\chi^2(1, N = 35) = 5.54$, $p < .05$. No significant differences were observed between PLT and WL, between EO and EPN, or between EPA and EPN.

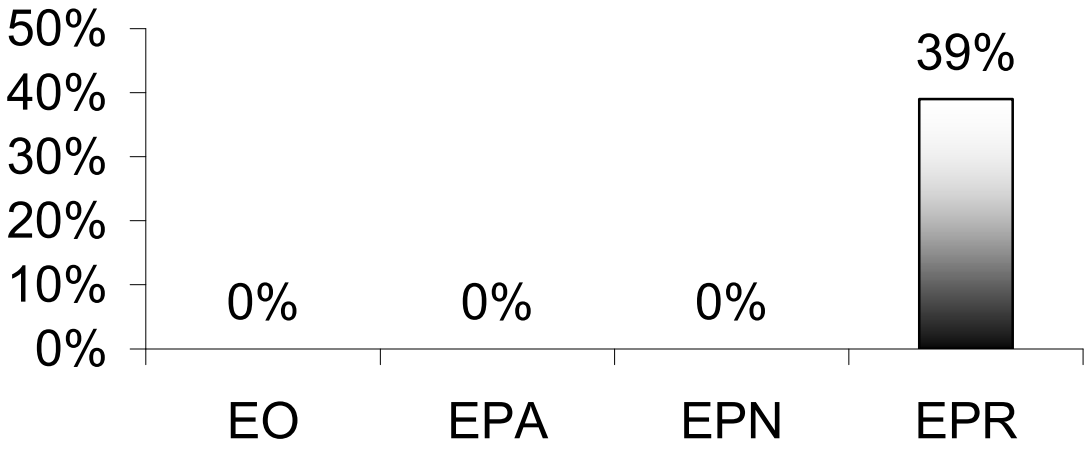


5.3.2.4 Follow-Up Return of Fear

Figure 3 presents data on the percentage of participants in each of the exposure conditions who met criteria for return of fear based on the reliable

change index (Jacobson & Truax, 1991). The percentage of participants meeting criteria for return of fear was as follows: EO=0%, EPA=0%, EPN=0% and EPR=39%. A chi-square analysis showed this difference was significant $\chi^2(3, N = 53) = 17.00$, $p < .001$.

Figure 3: FU Return of Fear



5.4 Moderator Analyses

No significant interactions were observed between any of the potential moderators and medication attribution factors. These findings suggest that the deleterious effects of medication attributions were not moderated by age, gender, marital status, ethnicity, or diagnostic status.

5.5 Mediation Analyses

5.5.1 Step 1: Effect of Treatment on the Mediator

In Step 1 we entered the scores on the Treatment Gain Attribution Questionnaire (Medication) as the DV and EPR vs. EPN as the grouping factor. Results indicated that the EPR group made significantly greater attributions to the positive effects of the medication compared to the EPN group, $F(1, 28) = 159.72$, $p<.000$.

5.5.2 Step 2: Effect of Treatment on Outcome

In Step 2 we entered the residualized change scores of peak fear from Post- to Follow-up during BAT 1 as the DV and EPR vs. EPN as the grouping factor. Results indicated that the EPR group showed significantly less improvement compared to the EPN group, $F(1, 32) = 14.95$, $p<.001$.

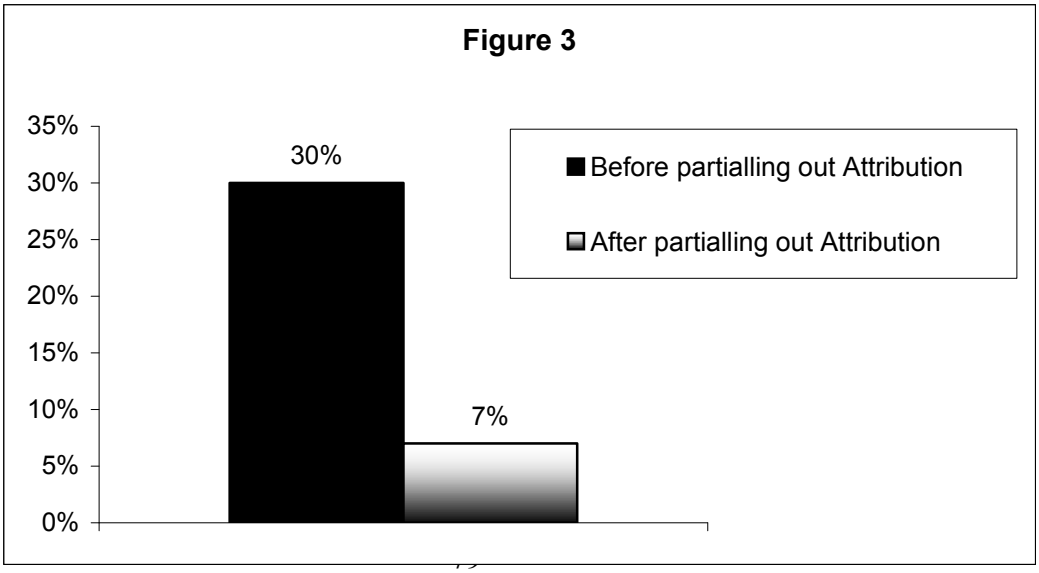
5.5.3 Step 3: Effect of the Mediator on Outcome

Next, in Step 3 we tested the effect of the mediator on outcome by regressing the residualized change scores of peak fear from Post- to Follow-up during BAT 1 on the scores from the Treatment Gain Attribution Questionnaire (Medication). The results showed that the medication attributions significantly predicted outcome, $F(2, 45) = 7.01$, $p<.01$.

5.5.4 Step 4: Effect of Treatment after Controlling for the Mediator

Finally, in Step 4 we tested the effect of treatment after controlling for medication attributions by entering the residualized change scores of peak fear from Post- to Follow-up during BAT 1 as the DV, EPR vs. EPN as the grouping factor, and the scores from the Treatment Gain Attribution Questionnaire (Medication) as a covariate. As predicted, the effects of treatment were no longer significant ($p>.05$). By controlling for medication attributions the percent variance accounted for by treatment was reduced from 30% to 7% (see Figure 3).

Figure 3



Percentage of variance in fear reduction accounted for by treatment before and after controlling for medication attributions and pre- to post- residualized change scores.

CHAPTER 6: DISCUSSION

Studies suggest that anxiety disorder patients who receive combined exposure-based and pharmacological treatment are at higher risk of relapsing if they discontinue their medication than if they receive CBT alone (Barlow, Gorman, Shear, & Woods, 2000). One reason may be that patients attribute their treatment gains to the positive effects of medication. In this way they learn conditional safety – I'm safe as long as I take my medication. The primary aim of the current study was to investigate the possible deleterious effects of these medication facilitation attributions on fear reduction during exposure-based treatment. Participants (N = 95) displaying marked claustrophobic fear were randomly assigned to 1 of 6 conditions: (a) Exposure Only (EO), (b) Exposure + Pill Placebo + Arousal Instruction (EPA: medication interference), (c) Exposure + Pill Placebo + Neutral Instruction (EPN), (d) Exposure + Pill Placebo + Relaxation Instruction (EPR: medication facilitation), (e) credible psychological placebo treatment (PLT), or (f) wait-list (WL). Medication attributions were manipulated after the posttreatment assessment thereby isolating the effects of attributions at follow-up and ruling out a straightforward placebo effect. Consistent with prediction belief in medication facilitation interfered with fear reduction at follow-up. However, contrary to prediction belief in medication interference did not enhance outcome at follow-up. The effect of taking medication with a neutral attribution had no effect on outcome. The placebo

group outperformed waitlist at posttreatment but not at follow-up. The exposure conditions did not outperform placebo at posttreatment but did at follow-up.

The waitlist condition showed steady improvement over the post- and follow-up assessments and is consistent with previous findings (Powers, Smits, & Telch, 2004). The waitlist condition provided a control for the effects of time and repeated assessments. The high performance among those participants in the placebo treatment condition at posttreatment and poor outcome at follow-up have at least two explanations possible. First, the placebo treatment device may have actually induced relaxation at posttreatment. However, the device was set at a frequency that is not consistent with relaxation according to previous research (Seiver, 2000). Second, there may have been a straightforward placebo effect due to the fact that these participants believed the flashing lights and sounds would induce relaxation at the posttreatment assessment followed by no such relaxation induction at the follow-up assessment. These findings are consistent with other studies from our laboratory (Powers, Smits, & Telch, 2004; Wolitzky & Telch, 2004) and highlight the importance of inclusion of such comparison conditions to control for the effects of time, repeated assessment, and expectancy.

Contrary to prediction the belief in medication interference (EPA) did not result in greater fear reduction. The manipulation check showed that although the EPA condition rated the harmful effects of medication higher than the other exposure conditions, they did not rate the helpful effects of treatment higher. This

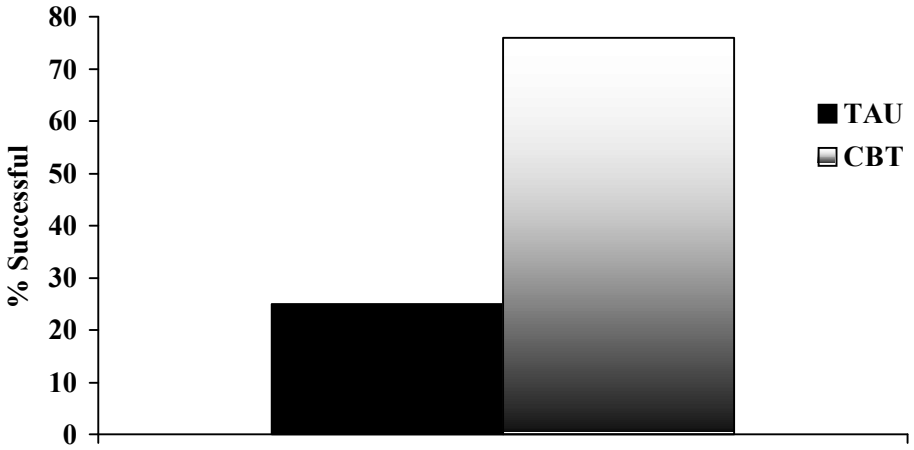
may represent a ceiling effect as both conditions rated treatment as highly effective. The findings suggest that attempts to augment exposure via concurrent administration of a stimulant may not succeed if the proposed mechanism is to enhance a belief in medication interference. As these participants did not receive an active medication it remains unclear to what extent concurrent stimulant administration would enhance fear reduction through other mechanisms.

Consistent with prediction enhancing a medication facilitation attribution (EPR) did interfere with fear reduction. Barlow et al. (2000) found a higher rate of relapse among patients who were on active medication while they received CBT for panic disorder when they later discontinued their medication than those who received CBT alone. Likewise, in a correlation study Biondi and Picardi (2003) found that 60% of patients who made positive attributions about medications during panic treatment relapsed compared to 0% of those who attributed their improvement to internal factors. This randomized clinical trial provides further support that making a positive attribution about medication during exposure treatment is a negative prognostic factor for outcome. During debriefing, participants reported that once they learned they had received a medication that facilitated their improvement, they were concerned about the upcoming follow-up assessment. They didn't seem to care how the "medication" had impacted their past but rather the implications for their future experiences in claustrophobic situations.

Contrary to prediction the exposure-based treatment did not significantly improve claustrophobic behaviors according to the Claustrophobic Behaviors Questionnaire. It is likely that this was due to the relatively short follow-up period. It may take more time to observe such changes. However, the primary aim of this study was not to assess the efficacy of claustrophobic exposure. In addition, analysis of the CBQ showed limited variability and a low baseline for the behaviors measured (i.e. Riding in the backseat of a car in the middle of two people). Also, the current CBQ reads, "Please rate the number of times you have engaged in the following behaviors over the previous week including today." The measure may be improved by increasing the time sample to, "over the previous month". During debriefing, patients largely reported that they were not sure how much the treatment would later impact their lives as they had not yet encountered claustrophobic situations. Later email correspondence with a limited number of participants suggested that they had in fact confronted more claustrophobic situation based on their participation. However, this sample is biased as it only included those who contacted us to thank us for participation.

The clinical implications of these findings suggest the importance of assessing attributions during exposure-based treatment of anxiety disorders. In practice we often ask three questions, (a) On a scale of 0 to 100%, how much improvement have you noticed in your symptoms?, (b) How much of this improvement do you feel is due to the medication?, and (c) How much of this

improvement do you feel is due to the treatment or your own efforts? The findings from this study suggest that the most effective intervention is to reduce the medication facilitation attributions (question b) rather than attempt to raise internal attributions by focusing on medication interference attributions (question c). One method that has proven effective is to conduct a slow taper off medications and to reapply CBT emphasizing interoceptive exposures and cognitive restructuring during the taper (see Figure; Otto, Jones, Craske, & Barlow, 1996; Otto, Pollack, & Barlow, 1995; Otto, Pollack, Sachs, Reiter, Meltzer-Brody, & Rosenbaum, 1993; Whittal, Otto, & Hong, 2001).



TAU=Treatment as Usual + Slow Taper

CBT=CBT + Slow Taper

For example, Otto et al. (1993) randomized 33 outpatients who had received a minimum of 6 months of benzodiazepine treatment for panic disorder to one of two taper conditions: a slow taper condition alone or a slow taper condition combined with 10 weeks of group cognitive-behavioral therapy. Patients who received CBT during the slow medication taper were more successful than patients who were in the slow taper only group (Otto et al., 1993). More specifically, 25% of those in the slow taper condition were successful compared to 76% in the slow taper plus CBT condition. At a 3-month follow-up, 77% of the patients in the CBT program remained medication free. As patients continue to apply exposure while going off of their medications they learn unconditional safety – I'm safe even when I don't take my medication. This medication discontinuation protocol has also been applied to SSRI treatment of panic disorder. In a case series Whittal et al. (2001) described the successful treatment of 8 participants who were being treated with an SSRI who wanted to discontinue their medication in the context of CBT. However, these studies do not address relapse prevention among patients who desire to stay on medication during CBT with a plan to later discontinue medication. If patients prefer to initiate or continue medication during CBT, relapse may continue to be a problem (Barlow et al. 2000). Future studies may explore the advantage of integrating the medication discontinuation strategies with such patients. In addition, these studies do not suggest *why* a slow taper and reapplication of CBT result in superior

outcome. Future studies may help determine if this slow taper/exposure combination changes medication attributions or operates through some other mechanism. Telch (in press) has also suggested that a single case double blind alternating treatment design helps patients overcome benzodiazepine attributions. A given patient is randomized to either placebo or benzodiazepine and they rate their anxiety each day. The therapist and patient then break the blind to determine how helpful the medication has been.

Several limitations deserve comment. First, although we used a stringent two-stage screening procedure to ensure that study participants displayed marked phobicity (our sample represented the top 1% on indices of claustrophobic fear and avoidance), 24% of the participants did not meet DSM-IV criteria for specific phobia. Among those who did not, all met full DSM-IV criteria with the exception of Criterion E (i.e., the person must experience significant interference in social, academic, or work functioning or experience marked distress about having the phobia). Therefore, the current study represents neither a strictly clinical nor analogue design. The current study, however, was designed to test the role of attributions about medication in the context of CBT rather than to determine the efficacy of exposure-based treatment. This hybrid design was selected to further investigate the potential moderating effects of clinical status. We examined empirically whether meeting all DSM-IV criteria moderated treatment outcome and it did not. This finding is consistent with our previous

study (Powers, Smits, & Telch, 2004) and provides additional evidence that those presenting with marked fear without significant life interference respond no differently to the treatments relative to those who are above diagnostic threshold. Second, although the EPA condition rated the harmful effects of medication higher than the other exposure conditions, they did not rate the helpful effects of treatment higher. Finally, the follow-up period of 1 week was too brief to make inferences about the stability of the attribution effects over the long term.

Future directions include identifying methods of reducing external attributions and enhancing internal attributions. It appears that a slow taper off medications while reapplying exposure may be effective in preventing relapse. It would be interesting to know if this effect is mediated by medication attributions. One method of enhancing fear reduction includes anti-phobic strategies (Wolitzky & Telch, 2004). Sloan and Telch (2001) proposed that the mere act of engaging in safety behaviors may directly activate the alarm system - much like there are direct neural pathways for sensorimotor information to travel to the limbic system (Ledoux, 1998). Hence, they hypothesized that actions that are not consistent with threat transmission may facilitate fear reduction achieved with exposure-based practice. Such inclusion of anti-phobic strategies involves more than eliminating safety behaviors; this is the active programming of behaviors that challenge the notion that one must be "careful" in a phobic situation. Preliminary evidence suggests that the inclusion of anti-phobic strategies in exposure-based

treatment protocols may indeed enhance outcome. For example, Wolitzky and Telch (2004) reported that participants with height phobia who employed anti-phobic actions such as jogging towards the railing, and making oneself dizzy near the railing, showed greater fear reduction compared to participants who completed exposure exercises as usual. From a learning perspective, anti-phobic strategies may function as "excitors" that increase the over prediction of the US thus resulting in a magnified discrepancy between the expectation of negative outcomes and the actual ("relatively safe") outcome achieved in exposure (Bouton, Mineka, & Barlow, 2001). Therefore, it is likely that the error correction and learning should also be magnified. However, it may also be the case that anti-phobic strategies enhance internal attributions – I must be safe if I can stay in the claustrophobic space even while taking caffeine. Although this study suggests that medication attributions are one path to potential relapse, it is likely that there are additional reasons. One such hypothesis is that what is learned on medication may not transfer to the non-drug state due to context effects (Powers, Smits, & Otto, in press). One solution may be pharmacological augmentation during exposure. Procedurally, exposure-based CBT is very similar to animal models of extinction of conditioned fears, and recent advances in animal research have identified pharmacological agents that appear to both accelerate and consolidate extinction learning (Cain, Blouin, & Barad, 2004; Davis, 2002). For example, administration of Yohimbine (an α2-receptor antagonist) during extinction trials accelerates fear

reduction and also may convert ineffective exposures to successful ones (Cain, Blouin, & Barad, 2004). In a series of studies, Cain et al. (2004) found that systemic administration (injection) of Yohimbine (5mg/kg) reduced the number of trials needed to extinguish fear in conditioned mice from 30 trials to only 5 trials. The facilitative effects of Yohimbine on fear reduction were also evident when the mice were later tested without the drug. Even more interesting, Yohimbine treated mice appeared to be protected from the negative effects of spacing extinction trials (20-minute intertrial intervals) compared to placebo treated mice. The effect of Yohimbine during exposure in humans has not yet been investigated.

In conclusion, results showed that a medication facilitation attribution (EPR: relaxing/sedating instruction) interfered with fear reduction. Contrary to prediction, a medication interference attribution (EPA: arousal instruction) did not enhance fear reduction compared to the other exposure conditions. The deleterious effects of the relaxation instructions were fully mediated by attributions about the helpful effects of the medication reducing the variance accounted for by treatment from 30% to 7%. Findings suggest the importance of assessing attributions during combined exposure-based and pharmacological treatments and attention to a slow medication taper and reapplication of exposure during the taper.

REFERENCES

Agras, S., Sylvester, D., & Oliveau, D. (1969). The epidemiology of common fears and phobias. *Comprehensive Psychiatry, 10,* 151-156.

Allgulander, C., & Lavori, P. W. (1991). Excess mortality among 3,302 patients with "pure" anxiety neurosis. *Archives of General Psychiatry, 48,* 599-602.

American Psychiatric Association (APA) (1994). *Diagnostic and statistical manual of mental disorders (4th ed.).* Washington, DC: Author.

American Psychiatric Association (APA) (1987). *Diagnostic and statistical manual of mental disorders (3rd ed.).* Washington, DC: Author.

Andrews, G., & Peters, L. (1998). The psychometric properties of the Composite International Diagnostic Interview. *Social Psychiatric & Psychiatric Epidemiology, 33,* 80-88.

Angst, J., Dobler-Mikola, A. (1985). The Zurich Study: V. Anxiety and phobia in young adults. *European Archives of Psychiatry and Neurological Sciences, 235,* 171-178.

Arntz, A., & Lavy, E. (1993). Does stimulus elaboration potentiate exposure in-vivo treatment? Two forms of one-session treatment of spider phobia. *Behavioral Psychotherapy, 21,* 1-12.

Antony, M.M., Swinson, R.P. (1996). *Anxiety disorders and their treatment: A critical review of the evidence-based literature.* Ottawa: Ontario. Health Canada, Minister of Supply and Services Canada.

Baker, B.L., Cohen, D.C., & Saunders, J.T. (1973). Self-directed desensitization for acrophobia. *Behaviour Research and Therapy, 11,* 79-89.

Barlow, D. H. (2002). *Anxiety and its disorders: The nature and treatment of anxiety and panic.* New York: Guilford Press.

Barlow, D. H. (1988). *Anxiety and its disorders: The nature and treatment of anxiety and panic.* New York: Guilford Press.

Barlow, D.H., Durand, V.M. (1995). *Abnormal psychology: An integrative approach.* (p. 706). Albany, NY: Brooks/Cole Publishing Company.

Barlow, D.H., Gorman, J.M., Shear, M.K., and Woods, S.W. (2000). Cognitive-behavioral therapy, imipramine, or their combination for panic disorder. *Journal of the American Medical Association, 283,* 2529-2536.

Basoglu, M., Marks, I.M., Kilic, C., Brewin, C.R. (1994). Alprazolam and exposure for panic disorder with agoraphobia attribution of improvement to medication predicts subsequent relapse. *British Journal of Psychiatry, 164,* 652-659.

Beck, A.T., Epstein, N., Brown, G., Steer, R.,A. (1988). An inventory for measuring clinical anxiety: Psychometric properties. *Journal of Consulting & Clinical Psychology, 56,* 893-897.

Beckham, J.C., Vrana, S.R., May, J.G., Gustafson, D.J., & Smith, G.R. (1990). Emotional processing and fear measurement synchrony as indicators of treatment outcome in fear of flying. *Journal of Behavior Therapy and Experimental Psychiatry, 21,* 153-162.

Benson H (1997): The nocebo effect: history and physiology. *Preventive Medicine 26*, 612-615.

Biondi, M., & Picardi, A. (2003). Attribution of improvement to medication and increased risk of relapse of panic disorder with agoraphobia. *Psychotherapy & Psychosomatics 72,* 110-111.

Blomhoff, S., Haug, T. T., Hellström, K., Holme, I., Humble, M., Madsbu, H.P., & Wold, J.E. (2001). Randomised controlled general practice trial of sertraline, exposure therapy and combined treatment in generalized social phobia. *British Journal of Psychiatry, 179,* 23-30.

Booth, R., & Rachman, S. (1992). The reduction of claustrophobia: I. *Behaviour Research and Therapy, 30,* 207-221.

Bootzin, R.R., Herman, C.P., & Nicassio, P. (1976). The power of suggestion: Another examination of misattribution and insomnia. *Journal of Personality and Social Psychology, 34,* 673-679.

Bourque, P., & Ladouceur, R. (1980). An investigation of various performance-based treatments with acrophobics. *Behaviour Research and Therapy, 18,* 161-170.

Candilis, P. J., McLean, R. Y., Otto, M. W., Manfro, G. G., Worthington, J. J. 3rd, Paneva, S. J., Marzol, P. C., Pollack, M. H. (1999). Quality of life in patients with panic disorder. *Journal of Nervous and Mental Disease, 187,* 429-434.

Clifford, C.A., Hopper, J.L., Fulker, D., & Murray, R.M. (1984). A genetic and environmental analysis of a twin family study of alcohol use, anxiety, and depression. *Genetic Epidemiology, 1,* 63-79.

Cohen, J. (1977). *Statistical power analysis for the behavioral sciences.* New York: Academic Press.

Cohen, J., & Cohen, P. (1983). *Applied multiple regression/correlation analysis for the behavioral sciences.* Hillsdale, NJ: Lawrence Erlbaum Associates.

Costello, C.G. (1982). Fears and phobias in women: A community study. *Journal of Abnormal Psychology, 91,* 280-286.

Cottraux, J., Mollard, E., Bouvard, M., Marks, I., Sluys, M., Nury, A.M., Douge, R., & Cialdella, P. (1990). A controlled study of fluvoxamine and exposure in obsessive-compulsive disorder. *International Clinical Psychopharmacology, 5,* 17-30.

Craske, M. (1999). *Anxiety Disorders.* Westview Press: Boulder, Colorado.

Craske, M.G., Mohlman, J., Yi, J., Glover, D., & Valeri, S. (1995). Treatment of claustrophobia and snake/spider phobias: Fear of arousal and fear of context. *Behaviour Research and Therapy, 33,* 197-203.

Craske, M.G., & Rowe, M.K. (1997). A comparison of behavioral and cognitive treatments for phobias. In G.C.L. Davey (Ed.), *Phobias: A handbook of theory, research, and treatment.* Chichester, England: Wiley.

de Jongh, A., Muris, P., ter Horst, G., & Duyx, M.P.M.A. (1995). Acquisition and maintenance of dental anxiety: The role of conditioning experiences and cognitive factors. *Behaviour Research and Therapy, 33,* 205-210.

de Jongh, A., Muris, P., ter Horst, G.T., van Zuuren, F., Schoenmakers, N., & Makkes, P. (1995). One-session cognitive treatment of dental phobia: Preparing dental phobics for treatment by restructuring negative cognitions. *Behaviour Research and Therapy, 33,* 947-954.

Devilly, G.J. & Borkovec, T.D. (2000). Psychometric properties of the credibility/expectancy questionnaire. *Journal of Behavior Therapy and Experimental Psychiatry, 31,* 73-86.

Di Nardo, P.A., Guzy, L.T., Jenkins, J.A., Bak, R.M., Tomasi, S.F., & Copland, M. (1988). Etiology and maintenance of dog fears. *Behaviour Research and Therapy, 26,* 241-244.

Eaton, W.W., Dryman, A., & Weissman, M.M. (1991). Panic and phobia. In L.N. Robins & D.A. Regier (Eds.), *Psychiatric disorders in America: The Epidemiological Catchment Area study.* New York: Free Press.

Edlund, M. J., & Swann, A. C. (1987). The economics and social costs of panic disorder. *Hospital and Community Psychiatry, 38,* 1277-1279, 1288.

Ehlers, A., Hofmann, S.G., Herda, C.A., & Roth, W.T. (1994). Clinical characteristics of driving phobia. *Journal of Anxiety Disorders, 8,* 323-339.

Emmelkamp, P.M.G., & Wessels, H. (1975). Flooding in imagination vs.

flooding in vivo: A comparison with agoraphobics. *Behaviour Research and Therapy, 13,* 7-15.

Fava, G. A., Savron, G., Zielezny, M., Grandi, S., Rafanelli, C., & Conti, S. (1997). Overcoming resistance to exposure in panic disorder with agoraphobia. *Acta Psychiatrica Scandinavica, 95,* 306-312.

Flint, J., Corley, R., DeFries, J.C., Fulker, D.W., Gray, J.A., Miller, S., & Collins, A.C. (1995). A simple genetic basis for a complex psychological trait in laboratory mice. *Science, 269,* 1432-1435.

Foa, E.B., Blau, J.S., Prout, M., & Latimer, P. (1977). Is horror a necessary component of flooding (implosion)? *Behaviour Research and Therapy, 15,* 397-402.

Franklin, M.E., Abramowitz, J.S., Bux, D.A., Zoellner, L.A., & Feeny N.C. (2002). Cognitive-behavioral therapy with and without medication in the treatment of obsessive-compulsive disorder. *Professional Psychology: Research and Practice, 33,* 162–168.

Fredrikson, M., Annas, P., & Wik, G. (1997). Parental history, aversive exposure and the development of snake and spider phobia in women. *Behaviour Research and Therapy, 35,* 23-28.

Fyer, A.J., Mannuzza, S., Gallps, M.S., Martin, L.Y., Aaronson, C., Borman, J.M., Leibowitz, M.R., & Klein, D.F. (1990). Familial transmission of simple phobias and fears. *Archives of General Psychiatry, 47,* 252-256.

Fydrich, T.,Dowdall, D., Chambless, D.L. (1992). Reliability and validity of the Beck Anxiety Inventory. *Journal of Anxiety Disorders, 6,* 55-61.

Gauthier, J., & Marshall, W.L. (1977). The determination of optimal exposure to phobic stimuli in flooding therapy. *Behaviour Research and Therapy, 15,* 403-410.

Getka, E.J., & Glass, C.R. (1992). Behavioral and cognitive-behavioral approaches to the reduction of dental anxiety. *Behavior Therapy, 23,* 433-448.

Gitin, N.M., Herbert, J.D., & Schmidt, C. (1996, November). One-session in vivo Exposure for ondontophobia. Paper presented at the 30th Annual Convention of the Association for Advancement of Behavior Therapy, New York.

Gould, R.A., Otto, M.W., & Pollack, M.H. (1995). A meta-analysis of treatment outcome for panic disorder. *Clinical Psychology Review, 15,* 819-844.

Greenberg, P.E., Sisitsky, T., Kessler, R.C., Finelstein, S.N., Berndt, E.R., Davidson, J.R., Ballenger, J.C., & Fyer, A.J. (1999). The economic burden of anxiety disorders in the 1990s. *Journal of Clinical Psychiatry, 60,* 427-435.

Greenberg, D.B., Stern, T.A., & Weilburg, J.B. (1988). The fear of choking: Three successfully treated cases. *Pychosomatics, 29,* 126-129.

Hahn R (1997): The nocebo phenomenon: Scope and foundations. In: Harrington A (Ed.): *The placebo effect*. Cambridge, Massachusetts: Harvard University Press. pp.56-75.

Hahn R (1997): The nocebo phenomenon: concept, evidence and implications for public health. *Preventive Medicine, 26,* 607-611.

Haug, T. T., Blomhoff, S., Hellström, K., Holme, I., Humble, M., Madsbu, H. P., & Wold, J. E. (2003). Exposure therapy and sertraline in social phobia: I-year follow-up of a randomised controlled trial. *British Journal of Psychiatry, 182,* 312-318.

Heffler, D. & Lisman, S.A. (1978). Attribution and insomnia: A replication failure. *Psychological Record, 28,* 123-128.

Heider, F. (1958). *The Psychology of Interpersonal Relations*. New York: Wiley.

Hellstrom, K., & Öst, L.-G. (1995). One-session therapist directed exposure versus two forms of manual directed self-exposure in the treatment of spider phobia. *Behaviour Research and Therapy, 33,* 959-965.

Hellstrom, K., Fellenius, J., & Öst, L.-G. (1996). One versus five sessions of applied tension in the treatment of blood phobia. *Behaviour Research and Therapy, 34,* 101-112.

Hepner, A., & Cauthen, N.R. (1975). Effect of subject control and graduated exposure on snake phobias. *Journal of Consulting and Clinical Psychology, 43,* 297-304.

Hofman, S.G. (in press). Cognitive mediation of treatment change in social phobia. *Journal of Consulting and Clinical Psychology.*

Hohagen, F., Winkelmann, G., Räsche-Rauschle, H., Hand, I., König, A., Münchau, N., Hiss, H., Geiger-Kabisch, C., Kappler, C., Schramm, P., Rey, E., Aldenhoff, J., & Berger, M. (1998). Combination of behaviour therapy with fluvoxamine in comparision with behaviour therapy and placebo. Results of a multicentre study. *British Journal of Psychiatry, 35*(Suppl), 71–78.

Holroyd, K.A. (1978). Effectiveness of an "Attribution Therapy" manipulation with test anxiety. *Behavior Therapy, 9,* 526-534.

Houlihan, D., Schwartz, C., Miltenberger, R., & Heuton, D. (1993). The rapid treatment of a young man's balloon (noise) phobia using in vivo flooding. *Journal of Behavior Therapy and Experimental Psychiatry, 24,* 233-240.

Howard, W.A., Murphy, S.M., & Clarke, J.C. (1983). The nature and treatment

of fear of flying: A controlled investigation. *Behavior Therapy, 14,* 557-567.

Jacobson, N., Truax, P. (1991). Clinical Significance: A statistical approach to defining meaningful change in psychotherapy research. *Journal of Consulting and Clinical Psychology, 59,* 12-19.

Jardine, R., Martin, N.G., and Henderson, A.S. (1984). Genetic covatioation between neuroticism and the symptoms of anxiety and depression. *Genetic Epidemiology, 1,* 89-107.

Jerremalm, A., Jansson, L., & Öst, L.G. (1986). Individual response patterns and the effects of different behavioral methods in the treatment of dental phobia. *Behaviour Research and Therapy, 24,* 587-596.

Kampman, M., Keijsers, G.P., Hoogduin, C.A., & Hendriks, G.J. (2002). A randomized, double-blind, placebo-controlled study of the effects of adjunctive paroxetine in panic disorder patients unsuccessfully treated with cognitive-behavioral therapy alone. *Journal of Clinical Psychiatry, 63,* 772-777.

Kellogg, R. & Baron, R.S. (1975). Attribution theory, insomnia, and the reverse placebo effect: A reversal of Storms and Nisbett's findings. *Journal of Personality and Social Psychology, 32,* 231-236.

Kendler, K.S., Karkowski, L.M., & Prescott, C.A. (1999). Fear and phobias: Reliability and heritability. *Psychological Medicine, 29,* 539-553.

Kendler, K.S., Neale, M.C., Kessler, R.C., Heath, A.C., & Eaves, L.J. (1992). The genetic epidemiology of phobias in women: The interrelationship of agoraphobia, social phobias, situational phobia, and simple phobia. *Archives of General Psychiatry, 49,* 273-281.

Kendler, K.S., Neale, M.C., Kessler, R.C., Heath, A.C., & Eaves, L.J. (1992). Major depression and generalized anxiety disorder: Same genes, (partly) different environments? *Archives of General Psychiatry, 49,* 716-722.

Kendler, K.S., Walters, E.E., Neale, M.C., Kessler, R.C., Heath, A.C., Eaves, L.J. (1995). The structure of the genetic and environmental risk factors for siz major psychiatric disorders in women: Phobia, generalized anxiety disorder, panic disorder, bulimia, major depression and alcoholism. *Archives of General Psychiatry, 52,* 374-383.

Kessler, R. C., Berglund, P., Demler, O., Jin, R., & Walters, E.E. (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Archives of General Psychiatry, 62,* 593-602.

Kessler, R.C., Chiu, W.T., Demler, O., & Walters, E.E. (2005). Prevalence,

severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Archives of General Psychiatry, 62,* 617-627.

Kessler, R.C., McGonagle, K.A., Zhao, S., Nelson, C.B., Hughes, M., Eshleman, S., Wittchen, H. U., & Kendler, K. S. (1994). Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States. *Archives of General Psychiatry, 51,* 8-19.

King, N.J., Clowes-Hollins, V., & Ollendick, T.H. (1997). The etiology of childhood dog phobia. *Behaviour Research and Therapy, 35,* 77.

Kleinknecht, R.A. (1994). Acquisition of blood, injury, and needle fears and phobias. *Behaviour Research and Therapy, 32,* 817-823.

Kraemer, H.C., Wilson, G.T., Fairburn, C.G., & Agras, W.S. (2002). Mediators and moderators of treatment effects in randomized clinical trials. *Archives of General Psychiatry, 59,* 877-883.

Leonard, K.N., Telch, M.J., Owen, K.K. (2000). Fear response to dissociation challenge. *Anxiety, Stress, & Coping, 13,* 355-369.

Leonard, K.N., Telch, M.J., Harrington, P.J. (1999). Dissociation in the laboratory: A comparison of strategies. *Behaviour Research & Therapy, 37,* 49-61.

Liddell, H.S. (1949). The role of vigilance in the development of animal neurosis. In P. Hoch & J. Zubin (eds.), *Anxiety.* New York: Grune & Stratton.

Lydiard, R.B., Brawman-Mintzer, O., & Ballenger, J.C. (1996). Recent developments in the psychopharmacology of anxiety disorders. *Journal of Consulting and Clinical Psychology, 64 (4),* 660-668.

MacKinnon, A.J., Henderson, A.S., & Andrews, G. (1990). Genetic and environmental determinants of the lability of traitneuroticism and the symptoms of anxiety and depression. *Psychological Medicine, 20,* 581-590.

Magee, W.J., Eaton, W.W., Wittchen, H.U., McGonagle, K.A., Kessler, R.C. (1996). Agoraphobia, simple phobia, and social phobia in the national comorbidity study. *Archives of General Psychiatry, 53,* 159-168.

Mannion, N.E., & Levine, B.A. (1984). Effects of stimulus representation and cure category level on exposure (flooding) therapy. *British Journal of Clinical Psychology, 23,* 1-7.

Markowitz, J. S., Weissman, M. M., Oullette, R., Lish, J. D., & Klerman, G. L. (1989). Quality of life in panic disorder. *Archives of General Psychiatry, 46,* 984-992.

Marks, I. (1978). Behavioural psychotherapy of adult neurosis. In S. Garfield & A.E. Bergin (Eds.), *Handbook of psychotherapy and behaviour modification.* Chichester: Wiley.

Marks, I.M., & Gelder, M.G. (1966). Different ages of onset in varieties of phobias. *American Journal of Psychiatry, 123,* 218-221.

Marks, I.M., Swinson, R.P., Basoglu, M., Kuch K., Noshirvani H., O'Sullivan G., Lelliott P.T., Kirby, M., McNamee, G., Sengun, S., et al. (1993). Alprazolam and exposure alone and combined in panic disorder with agoraphobia. A controlled study in London and Toronto. *British Journal of Psychiatry, 162,* 776-87.

Mavissikalian, M., & Perel, J.M. (1993). Clinical experience in maintenance and discontinuation of imipramine therapy in panic disorder with agoraphobia. *Archives General Psychiatry, 49,* 318-323.

McNally, R.J., & Steketee, G.S. (1985). The etiology and maintenance of severe animal phobias. *Behaviour Research and Therapy, 23,* 431-435.

Menzies, R., G., & Clarke, J. C. (1993a). The etiology of fear of heights and its relationship to severity and individual response patterns. *Behaviour Research and Therapy, 31,* 9-15.

Menzies, R.G., & Clarke, J.C. (1993b). A comparison of in vivo and vicarious exposure in the treatment of childhood water phobia. *Behaviour Research and Therapy, 31,* 9-15.

Merchelbach, H., Arntz, A., & de Jong, P. (1991). Conditioning experiences and spider phobics. *Behaviour Research and Therapy, 29,* 333-335.

Merchelbach, H., Arntz, A., Arrindell, W.A., & de Jong, P.J. (1992). Pathways to spider phobia. *Behaviour Research and Therapy, 30,* 543-546.

Merchelbach, H., & Muris, P. (1997). The etiology of childhood spider phobia. *Behaviour Research and Therapy, 35,* 1031-1034.

Moore, R., & Brodsgaard, I. (1994). Group therapy compared with individual desensitization for dental anxiety. *Community Dentistry and Oral Epidemiology, 22,* 258-262.

Moore, R., Brodsgaard, I., & Birn, H. (1991). Manifestations, acquisition and diagnostic categories of dental fear in a self-referred population. *Behaviour Research and Therapy, 29,* 51-60.

Munjack, D. (1984). The onset of driving phobias. *Journal of Behavior Therapy and Experimental Psychiatry, 15,* 305-308.

Muris, P., Mayer, B., & Merckelbach, H. (1998). Trait anxiety as a predictor of

behaviour therapy outcome in spider phobia. *Behavioural and Cognitive Psychotherapy, 26,* 87-91.

Muris, P., Merchelbach, H., & Collaris, R. (1997). Common childhood fears and their origins. *Behaviour Research and Therapy, 35,* 929-937.

Muris, P., Merckelbach, H., Holdrinet, I., & Sijsenaar, M. (1998). Treating phobic children: Effects of EMDR versus exposure. *Journal of Consulting and Clinical Psychology, 66,* 193-189.

Muris, P., Merckelbach, H., van Haaften, H., & Mayer, B. (1997). Eye movement desensitization and reprocessing versus exposure in vivo: A single-session crossover study of spider-phobic children. *British Journal of Psychiatry, 171,* 82-86.

Muris, P., Steerneman, P., Merckelback, H., & Meesters, C. (1996). The role of parental fearfulness and modeling in children's fear. *Behaviour Research and Therapy, 34,* 265-268.

Noyes, R., Garvey, M.J., Cook, B.L., & Samuelson, L. (1989). Problems with tricyclic antidepressant use in patients with panic disorder or agoraphobia: results of a naturalistic follow-up study. *Journal of Clinical Psychiatry, 50,* 163-169.

Noyes, R. Garvey, M.J. Cook, B. & Suelzer, M. (1991). Controlled discontinuation of benzodiazepine treatment for patients with panic disorder. *American Journal of Psychiatry, 148,* 517-523.

Öst, L.-G. (1978). Behavioral treatment of thunder and lightening phobias. *Behaviour Research and Therapy, 16,* 197-207.

Öst, L.-G. (1985). Mode of acquisition of phobias. *Acta Universitatis Uppsaliensis (Abstracts of Uppsala Dissertations for the Faculty of Medicine), 529,* 1-45.

Öst, L.-G. (1987). Age of onset in different phobias. *Journal of Abnormal Psychology, 96,* 223-229.

Öst, L.-G. (1991). Acquisition of blood and injection phobia and anxiety response patterns in clinical patients. *Behaviour Research and Therapy, 29,* 323-332.

Öst, L.-G. (1996a). Long-term effects of behavior therapy for specific phobia. In M. R. Mavissakalian & R. F. Prien (Eds.), *Long-term treatments of anxiety disorders* (pp. 121-170). Washington, DC: American Psychiatric Press.

Öst, L.-G. (1996b). One-session group treatment of spider phobia. *Behaviour Research and Therapy, 34,* 707-715.

Öst, L.-G., Brandberg, M., & Alm, T. (1997). One versus five sessions of exposure in the treatment of flying phobia. *Behaviour Research and Therapy, 35,* 987-996.

Öst, L.-G., Fellenius, J., & Sterner, U. (1991). Applied tension, exposure in vivo, and tension only in the treatment of blood phobia. *Behaviour Research and Therapy, 29,* 561-574.

Öst, L.-G., Ferebee, I., & Furmark, T. (1997). One session group therapy of spider phobia: Direct versus indirect treatments. *Behaviour Research and Therapy, 35,* 721-732.

Öst, L.G., Hellstrom, K. & Kraver, A. (1992). Blood and injection phobia: Background and cognitive, physiological, and behavioral variables. *Journal of Abnormal Psychology, 101,* 68-74.

Öst, L.-G., Hellstrom, K., & Kaver, A. (1992). One versus five sessions of exposure in the treatment on injection phobia. *Behaviour Research and Therapy, 23,* 263-282.

Öst, L.-G., & Hugdahl, K. (1981). Acquisition of phobias and anxiety response patterns in clinical patients. *Behaviour Research and Therapy, 19,* 439-447.

Öst, L.-G., & Hugdahl, K. (1985). Acquisition of blood and dental phobia and anxiety response patterns in clinical patients. *Behaviour Research and Therapy, 23,* 27-34.

Öst, L.-G., Johansson, J., & Jerremalm, A. (1982). Individual response patterns and the effects of different behavioral methods in the treatment of claustrophobia. *Behaviour Research and Therapy, 20,* 445-460.

Öst, L.-G., Lindahl, I.-L., Sterner, U., & Jerremalm, A. (1984). Exposure in vivo vs. applied relaxation in the treatment of blood phobia. *Behaviour Research and Therapy, 22,* 205-216.

Öst, L.-G., Salkovskis, P. M., & Hellstrom, K. (1991). One-session therapist directed exposure versus self-exposure in the treatment of spider phobia. *Behavior Therapy, 22,* 407-422.

Öst, L.-G., Sterner, U., & Fellenius, J. (1989). Applied tension, applied relaxation, and the combination in the treatment of blood phobia. *Behaviour Research and Therapy, 27,* 109-121.

Otto, M.W., Jones, J.C., Craske, M.G., Barlow, D.H. (1996). *Stopping anxiety medication: Panic control therapy for benzodiazepine discontinuation (Therapist Guide).* San Antonio, TX: Psychological Corporation.

Otto, M.Q., Pollack, M.H., Barlow, D.H. (1995). *Stopping Anxiety Medication: A workbook for patients wanting to discontinue benzodiazepine treatment for*

panic disorder. San Antonio, TX: Psychological Corporation.

Otto, M. W., Pollack, M. H., Penava, S. J., & Zucker, B. G. (1999). Cognitive-behavior therapy for patients failing to respond to pharmacotherapy for panic disorder: A clinical case series. *Behaviour Research and Therapy, 37,* 763-770.

Otto, M.W., Pollack, M.H., Sachs, G.S., Reiter, S.R., Meltzer-Brody, S., & Rosenbaum, J.F. (1993). Discontinuation of benzodiazepine treatment: Efficacy of cognitive-behavior therapy for patients with panic disorder. *American Journal of Psychiatry, 150,* 1485-1490.

Panzarella, C., & Garlipp, J. (1999). Integration of cognitive techniques into an individualized application of behavioral treatment of blood-injection-injury phobia. *Cognitive and Behavioral Practice, 6,* 200-211.

Pollack M.H., Otto, M.W., Kaspi, S.P., Hammerness, P.G., & Rosenbaum, J.F. (1994). Cognitive-behavior therapy for treatment-refractory panic disorder. *Journal of Clinical Psychiatry, 55,* 200-205.

Pollack, M.H., & Smoller, J.W. (1996). Pharmacologic approaches to treatment resistant panic disorder. In: Pollack MH, Otto MW, (Eds.), *Challenges in Clinical Practice: Pharmacological and Psychosocial Strategies* (pp. 89-112). New York: Guildford, 1996.

Pollard, C. A., Henderson, G., Frank, M., & Margolis, R. B. (1989). Help-seeking patterns of anxiety-disordered individuals in the general population. *Journal of Anxiety Disorders, 3,* 131-138.

Porges, S. (1995). Cardiac vagal tone: A physiological index of stress. *Neuroscience and Biobehavioral Reviews. 19,* 225-233.

Power, K. G., Simpson, R. J., Swanson, V., & Wallace, L. A. (1990). Controlled comparison of pharmacological and psychological treatment of generalized anxiety disorder in primary care. *British Journal of General Practice, 40*(336), 289-294.

Powers, M.B., Smits, J., Leyro, T. M., & Otto, M. (in press). Translational research perspectives on maximizing the effectiveness of exposure therapy. In D. C. S. Richard & D. Lauterbach (Eds.), *Comprehensive Handbook of the Exposure Therapies.* Academic Press.

Powers, M., Smits, J., & Telch, M. (2004). Disentangling the effects of safety behavior utilization and availability during exposure-based treatment: A placebo-controlled study. *Journal of Consulting and Clinical Psychology, 72,* 448-454.

Rachman, S.J. (1976). The passing of the two-stage theory of fear and avoidance:

Fresh possibilities. *Behaviour Research and Therapy, 14,* 125-387.

Rachman, S.J. (1977). The conditioning theory of fear acquisition: A critical examination. *Behaviour Research and Therapy, 15,* 375-387.

Rachman, S. (1990). *Fear and courage (2nd ed.).* New York: Freeman.

Rachman, S., & Taylor, S. (1993). Analyses of Claustrophobia. *Journal of Anxiety Disorders, 7,* 281-291.

Radomsky, A.S., Rachman, S., Thordarson, D.S., McIsaac, H.K., Teachman, B.A. (2001). The Claustrophobia Questionnaire. *Journal of Anxiety Disorders, 15,* 287-297.

Rice, D. P.; & Miller, L. S. (1993). The economic burden of mental disorders. *Advances in Health Economics and Health Services Research, 14,* 37-53.

Rimm, D.C., Janda, L.H., Lancaster, D.W., Nahl, M., & Dittmar, K. (1977). An exploratory investigation of the origin and maintenance of phobias. *Behaviour Research and Therapy, 15,* 231-238.

Salkovskis, P.M. (1991). The importance of behaviour in the maintenance of anxiety and panic: A cognitive account. *Behavioural Psychotherapy, 19,* 6-19.

Salkovskis, P.M., Clark, D.M., Hackman, A., Wells, A., & Gelder, M.G. (1999). An experimental investigation of the role of safety behaviours in the maintenance of panic disorder with agoraphobia. *Behaviour Research & Therapy , 37,* 559-574.

Sanderson, A., & Carpenter, R. (1992). Eye movement desensitization versus image confrontation: A single-session crossover study of 58 phobic subjects. *Journal of Behavior Therapy and Experimental Psychiatry, 23,* 269-275.

Shapiro, F., & Forrest, M.S. (1997). *EMDR: The breakthrough therapy for overcoming anxiety, stress, and trauma.* New York, NY: Basic Books.

Shapiro AK & Shapiro E (1997a): *The Powerful Placebo – from ancient priest to modern physician.* Baltimore, MD: The John Hopkins University Press.

Shapiro AK & Shapiro E (1997b): The placebo: much ado about nothing? In: Harrington A (Ed.): *The placebo effect.* Cambridge, Massachusetts: Harvard university press. pp.13-35.

Sheehan, D.V., Sheehan, K.E., & Minichiello, W.E. (1981). Age of onset of phobic disorders: A reevaluation. *Comprehensive Psychiatry, 22,* 544-553.

Siever, D. (2000). *The Rediscovery of Audiovisual Entrainment Technology.* Edmonton, Alberta, Canada: Comptronic Devices Limited.

Singerman, K.J., Borkovec, T.D., Baron, R.S. (1976). Failure of a

"Misattribution Therapy" Manipulation with a clinically relevant target behavior. *Behavior Therapy, 7,* 306-313.

Sloan, T., Telch, M.J. (2001). The effects of safety-seeking behavior and guided threat reappraisal on fear reduction during exposure: An experimental investigation. *Behaviour Research & Therapy, 40,* 235-251.

Smits, J., Powers, M., Cho, Y., & Telch, M. (2004). Mechanism of change in cognitive-behavioral treatment of panic disorder: Evidence for the anxiety sensitivity mediational hypothesis. *Journal of Consulting and Clinical Psychology, 72,* 646-652.

Spielberger, C.D., Gorsuch, R.L., & Lushene, R.E. (1970) . *The State Trait Anxiety Inventory.* Palo Alto, CA: Consulting Psychologists Press.

Storms, M.D., & Nisbett, R.E. (1970). Insomnia and the attribution process. *Journal of Personality and Social Psychology, 16,* 319-328.

Telch, M. (1988). Antidepressant medication and psychotherapy in the treatment of panic: A critical review. In S.J. Rachman, & J.D. Maser. (Eds.) *Panic: Psychological perspectives.* Hillsdale, NJ: Lawrence Erlbaum Associates, Inc.

Telch, M. J., Agras, W. S., Taylor, C. B., Roth, W. T., & Gallen, C. (1985). Combined pharmacological and behavioral treatment for agoraphobia. *Behaviour Research and Therapy, 23,* 325-335.

Telch, M. J., & Lucas, R.A. (1994). Combined pharmacological and psychological treatment of panic disorder: Current status and future directions. In: B.E. Wolfe & J.D. Maser (Eds.) *Treatment of panic disorder* (pp. 177-197). American Psychiatric Association Press,Washington DC.

Telch, M., Sloan, Smits, J., Powers, M., Horowitz, & Wolitzky (2005). Safety Behavior Fading in the Treatment of Panic Disorder. *Manuscript in preparation.*

Telch, M.J., Tearnan, B.H., & Taylor, C.B. (1983). Antidepressant medication in the treatment of agoraphobia: A critical review. *Behavior Research and Therapy, 21,* 505-517.

Telch, M., Valentiner, D., Ilai, D., Young, P., Powers, M., Smits, J. (2005). Fear Activation and Distraction during the Emotional Processing of Claustrophobic Fear. *Journal of Behavior Therapy and Experimental Psychiatry, 35,* 219-232.

Thompson, J. W., Burns, B. J., Bartko, J. J., Boyd, J. H., Taube, C. A., & Bourden, K. H. (1988). The use of ambulatory services by persons with and without phobia. *Medical Care, 26,* 183-198.

Thyer, B.A., Parrish, R.T., Curtis, G.C., Nesse, R.M., & Cameron, O.G. (1985). Ages of onset of DSM-III anxiety disorders. *Comprehensive Psychiatry, 26,*

113-121.

Townend, E., Dimigen, G., & Fung, D. (2000). A clinical study of child dental anxiety. *Behaviour Research and Therapy, 38,* 31-46.

Uhl, G.R., Gold, L.H., & Risch, N. (1997). *Genetic analyses of complex behavioral disorders.* Proceedings of the National Academy of Sciences USA, 94, 2785-2786.

Valentiner, D.P., Telch, M.J., Petruzzi, D., & Bolte, M. (1996). The cognitive determinants of claustrophobic reactions: Reiss and McNally's expectancy model and Bandura's self-efficacy theory. *Cognitive Therapy and Research, 20,* 593-612.

van Balkom, A.J., de Haan, E., van Oppen, P., Spinhoven, P., Hoogduin, K.A., & van Dyck, R. (1998). Cognitive and behavioral therapies alone and in combination with fluvoxamine in the treatment of obsessive compulsive disorder. *Journal of Nervous and Mental Disease, 186,* 492–499.

Verburg, C., Griez, E., & Meijer, J. (1994). A 35% carbon dioxide challenge in simple phobias. *Acta Psychiatrica Scandanavica, 90,* 420-423.

Wells, A., Clark, D.M., Salkovskis, P., Ludgate, J., Hackmann, A., Gelder, M. (1995). Social phobia: The role of in situation safety behaviors in maintaining anxiety and negative beliefs. *Behavior Therapy, 26,* 153 161.

Whittal, M.L., Otto, M.W., & Hong, J.J. (2001). Cognitive-behavior therapy for discontinuation of SSRI treatment of panic disorder: A case series. *Behaviour Research & Therapy, 39,* 939-945.

Willerman, L., & Cohen, D.B. (1990). *Psychopathology.* New York: McGraw-Hill Publishing Company.

Wiliams, S. L., Dooseman, G., Kleifield, E. (1984). Comparative effectiveness of guided mastery and exposure treatments for intractable phobias. *Journal of Consulting & Clinical Psychology, 52,* 505-518.

Wittchen, H. U. (1988). Natural course and spontaneous remissions of untreated anxiety disorder: Results of the Munich Follow-up study (MFS). In H. Hand, H., & H. Wittchen (Eds.), *Panic and phobias: Treatments and variables affecting course and outcome (pp. 3-17).* Berlin: Springer-Verlag.

Wolitzky, K.B. & Telch, M.J. (in preparation). Placebo-controlled trial investigating the efficacy of encouraging anti-phobic actions during in vivo exposure treatment for acrophobia.

Wolpe, J. (1958). Psychotherapy by reciprocal inhibition as the main basis of psychotherapeutic effects. *Archives of Neurology and Psychiatry, 72,* 205.

Wolpe, J. (1973). *The practice of behavior therapy (2nd ed.)*. New York: Pergamon Press.

VITA

Mark Bradley Powers was born in Los Angeles California on May 26, 1971, the son of Allen and Joanie Powers. After completing high school at El Camino, Woodland Hills, California in 1989, he entered the University of California at Santa Barbara. He received his Bachelor of Arts degree in psychology in June 1996. In September 1996, he entered the Graduate Psychology Program at Pepperdine University where he received his Master's Degree in June 1997. He entered the Graduate School of the University of Texas at Austin in August 2001. During the academic year of 2005-2006, he completed a pre-doctoral clinical internship at Washington University Medical Center.

Permanent Address: 24862 Wooded Vista Drive, West Hills, CA 91307.

This dissertation was typed by the author.